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	antibodies and agonists or antagonists of	of nephropathy and/or other diseases and disorders as
	the invention) to stimulate insulin	
	secretion. For example, insulin secretion	
	is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
	insulin antibodies. Insulin secretion from	
	pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
	glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
	proteins/peptides, and disregulation is a	
	key component in diabetes. Exemplary	
	assays that may be used or routinely	stroke, and other diseases and disorders as described in the
	modified to test for stimulation of insulin	
	secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
	polypeptides of the invention (including	
	antibodies and agonists or antagonists of	
	the invention) include assays disclosed in:	<u>.</u>
	Ahren, B., et al., Am J Physiol, 277(4 Pt	
	2):R959-66 (1999); Li, M., et al.,	
	Endocrinology, 138(9):3735-40 (1997);	
	Kim, K.H., et al., FEBS Lett, 377(2):237-9	
	(1995); and, Miraglia S et. al., Journal of	
	Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications i
	(1999), the contents of each of which is	
	herein incorporated by reference in its	highly preferred indications are complications associated
	entirety. Pancreatic cells that may be used	sed with insulin resistance.
	according to these assays are publicly	
,	available (e.g., through the ATCC) and/or	/or
	may be routinely generated. Exemplary	A
	pancreatic cells that may be used	
	according to these assays include rat INS-1	[3-1]
	cells. INS-1 cells are a semi-adherent cell	les
	line established from cells isolated from an	nan
	X-ray induced rat transplantable	
	insulinoma. These cells retain	
	characteristics typical of native pancreatic	ıtic
	beta cells including glucose inducible	
	insulin secretion. References: Asfari et al.	it al.
	Endocrinology 1992 130:167.	

A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An alternative highly preferred embodiment of the invention includes a method for decreasing adipocyte survival. A preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Preferred indications include neoplastic diseases (e.g.,	lipomas, liposarcomas, and/or as described below under "Hyperproliferative Disorders"), blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Infectious Diseases"). An difficial Activity and Neurological Diseases"), and infection (e.g., as described below under "Infectious Diseases"). An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g. due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy, sizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart
Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including artibodies and aconists or antaconists of	the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.
Activation of Adipocyte Pl3 Kinase Signalling Pathway	·
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disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuyren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma, liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to
	Activation of Adipocyte Kinase assay ERK Signaling an Elk-1 king transduction or differentia and may be u
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					"Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications associated with insulin resistance. Additional highly preferred indications associated with insulin resistance. Additional highly preferred indications as described herein. Additional highly preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or
21	HAOAG15	535	Activation of Natural Killer Cell ERK Signaling Pathway.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	dysplasia. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention

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	immune cells (such as mast cells).	differentiation, are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the	and/or treatment of asthma, allergy, hypersensitivity and inflammation.

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			immune cell function, modulate B cell Ig	preferred indication includes rhinitis. An additional
			production, modulate immune cell	n (e
			polarization, and/or mediate humoral or	disease as described below under "Infectious Disease"),
			cell-mediated immunity. Exemplary	and inflammation and inflammatory disorders.
			assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
			proteins evaluate the production of	described below under "Immune Activity", "Blood-
			cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
			stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
			cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
			be used or routinely modified to test	multiple sclerosis and/or as described below) and
			immunomodulatory activity of	immunodeficiencies (e.g., as described below).
			polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
			antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
			the invention) include the assays disclosed	below under "Hyperproliferative Disorders"). Preferred
			in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
			Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
			al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
			Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include
			Blood 92(9):3338-3345 (1998); Jung et al.,	benign dysproliferative disorders and pre-neoplastic
			Eur J Immunol 25(8):2413-2416 (1995);	conditions, such as, for example, hyperplasia, metaplasia,
			Mori et al., J Allergy Clin Immunol 106(1	and/or dysplasia. Preferred indications include anemia,
			Pt 2):558-564 (2000); and Koning et al.,	pancytopenia, leukopenia, thrombocytopenia, leukemias,
			Cytokine 9(6):427-436 (1997), the	Hodgkin's disease, acute lymphocytic anemia (ALL),
			contents of each of which are herein	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
			incorporated by reference in its entirety.	arthritis, AIDS, granulomatous disease, inflammatory
			Human T cells that may be used according	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
			to these assays may be isolated using	immune reactions to transplanted organs and tissues,
			techniques disclosed herein or otherwise	hemophilia, hypercoagulation, diabetes mellitus,
			known in the art. Human T cells are	endocarditis, meningitis, and Lyme Disease.
			primary human lymphocytes that mature in	
			the thymus and express a T cell receptor	
			and CD3, CD4, or CD8. These cells	
			mediate humoral or cell-mediated	
			immunity and may be preactivated to	
			enhance responsiveness to	
			immunomodulatory factors.	
24 HATBI94	538	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention

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				presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
24	HATBI94	538	Production of TNF	TNFa FMAT. Assays for	
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-
				routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
				polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
				antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
				immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
				inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
				assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
***				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
				alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
				inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
				response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
				routinely modified to test	leukemia, lymphoma, and/or as described below under
				immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
				polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
				antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
				Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
				4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
				"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
				Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
				al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
				(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				Nardelli et al., J Leukoc Biol 63:822-828	granulomatous disease, initaminatory bower disease,

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				(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
				herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
				entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
				be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
				isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
				or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
				dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
				in suspension culture, which, when	Disease").
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
				and functional activities.	
25	HATCB45	539	Upregulation of CD152	CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention
			and activation of T cells	expression is restricted to activated T cells.	includes a method for activating T cells. An alternative
				CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				proliferation. Reduced CD152 expression	method for inhibiting the activation of and/or inactivating
				has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
				autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
				CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
				immunoresponses. Assays for	of the invention includes a method for stimulating T cell
				immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
				expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
				CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications
				may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
				assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
				invention (including antibodies and	described below), immunodeficiencies (e.g., as described
				agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
				modulate the activation of T cells,	suppressing a T cell-mediated immune response.
				maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
				immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
		-		Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
		*****		modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for

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				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
26	HATCD80	540	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the

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modified to test for stimulation of insulin secretion (from pancreatic cells) by perpetudes of the invention (including antibodies and agonists or antagonists of the invention) included assays disclosed in Shimizu, H., et al., Endocr. J. 47(3):261-9 (isabetic retinopathy and bindness), ulcers and the invention) include assays disclosed in Shimizu, H., et al., Endocr. J. 47(3):261-9 (isabetic retinopathy and bindness), ulcers and invention of including and significance and agonists or antagonists of inpaired wound healing, and infectious (e.g., infectious (2000), Salapatek, A.M., et al., Mol Biolochina, J. 3(8):1305-11 (1999); and margin see. a. J. (1999). (sometime invention) include assays disclosed in Skin), carpal tumel syndrome and Dupuytren's Flipsson, K., et al., Ann N Y Acad Sci, Sci, A. 21 (1999), the contracture). An additional highly preferred indications include Miragin's et al., Durand of Blomolecular weight loss or alternatively, weight gain. Additional Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by referred instructively parcreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epitheial cell line established from Syrian hamsteristle cells transformed with SV40. The cells express glucagon, somatostatin, and glucocorticoid receptors. The cells express glucagon and suppressed by somatostatin, and glucocorticoid receptors. And Actor Blochem. 1. 219: 6-45 st. Local and Actor Blochem. 1. 219: 6-45 st. Local and an advanced to the stable of the stable o	Activation of Skeletal Kinase assay. Kinase assay, for PI3 kinase Signalling Pathway Signalling Pathway Sci. USA 78: 4339-4343, 1981. Activation of Skeletal Kinase assay. Kinase assay, for PI3 kinase includes a method for includes a method for decreasing muscle cell survival are well-
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routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.		ell proliferation. In a uscle cell proliferation is preferred embodiment of for inhibiting muscle cell odiment, skeletal muscle embodiment, skeletal muscle embodiment, skeletal nulated. An alternative the invention includes a ll differentiation. In a uscle cell differentiation is breferred indications. Preferred indications include disorders Preferred indications of a seasoribed below under "Neural Activity ood disorders (e.g., as the crime of season o
·	described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease,	rs" section below), diabetic erve damage (e.g., due to sel blockage, heart disease, iabetic neuropathy or , mental confusion, cemic-hyperosmolar g., heart disease,
	atherosclerosis, microvascular disease, hypertension,	isease, hypertension,

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<u> </u>	of the invention includes a method for activating NK cells.	-
polypeptides of the invention (including	An alternative highly preferred embodiment of the	
antibodies and agonists or antagonists of i	invention includes a method for inhibiting activation of	
Jo t	and/or inactivation NK cells. Highly preferred	
T cells, and/or mediate humoral or cell-	indications include inflammation and inflammatory	
	disorders (e.g., as described below under "Immune	
	Activity"). Preferred indications include blood	
evaluate the upregulation of cell surface	disorders (e.g., as described below under "Immune	
	Activity", "Blood-Related Disorders", and/or	
	Cardiovascular Disorders"). Highly preferred indications	
or routinely modified to test	nclude autoimmune diseases (e.g., rheumatoid arthritis,	
immunomodulatory activity of s	ystemic lupus erythematosis, multiple sclerosis and/or as	
including	escribed below), immunodeficiencies (e.g., as described	
•	elow), boosting a T cell-mediated immune response and	
	Iternatively suppressing a T cell-mediated immune	
	esponse, and boosting a B cell-mediated immune	
(1999);	esponse and alternatively suppressing a B cell-mediated	
	mmune response. An additional highly preferred	-
	ndication includes infection (e.g., as described below	
	nder "Infectious Disease"). Preferred indications also	
(200); Werfel et al., Allergy 52(4):465-469 ii		
	arombocytopenia, Hodgkin's disease, acute lymphocytic	
	nemia (ALL), plasmacytomas, multiple myeloma,	
	urkitt's lymphoma, arthritis, AIDS, granulomatous	
460 (1993), the contents of each of which d	isease, inflammatory bowel disease, sepsis, neutropenia,	
	eutrophilia, psoriasis, suppression of immune reactions to	
	ansplanted organs and tissues, hemophilia,	
lated	ypercoagulation, diabetes mellitus, endocarditis,	
	neningitis, Lyme Disease, inflammation and	
r cells	nflammatory disorders, asthma, and allergies.	
	referred indications also include neoplastic diseases (e.g.,	
mature in the thymus and express a T Cell 1.	sukemia, lymphoma, and/or as described below under	
receptor and CD3, CD4, or CD8. These	Hyperproliferative Disorders"). Preferred indications	
cells mediate humoral or cell-mediated	nclude neoplasms, such as, for example, leukemia,	
immunity and may be preactivated to	/mphoma, and prostate, breast, lung, colon, pancreatic,	
enhance responsiveness to	sophageal, stomach, brain, liver and urinary cancer.	
markers, such as of T cells. Such or routinely moc immunomodulat polypeptides of antibodies and a the invention) in assays disclosed Biomolecular Sc Rowland et al., approach." Chay Ferenczi et al., approach." Chay Ferenczi et al., approach." (1997); Taylor-I Immunol 25(12) Afetra et al., An 460 (1993), the are herein incorpentirety. Human according to the using techniques otherwise know are primary hum mature in the thy receptor and CD cells mediate hum immunity and matume respons	; 0 v	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis andor as described below), boosting a T cell-mediated immune response and alternatively suppressing a T cell-mediated immune response and alternatively suppressing a B cell-mediated immune response. An additional highly preferred indication includes infection (e.g., as described below under "Infectious Disease"). Preferred indications also include anemia, pancytopenia, leukopenia, hrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, hrombocytopenia, hombocytopenia, hemophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, edisease, inflammatory disorders, asthma, and allergies. T cells that may be used season of inthe art. Human T cells meningitis, Lyme Disease, inflammation and hymbocytes that may be isolated meningitis, Lyme Disease, inflammation and acspress a T Cell "Hyperproliferative Disorders"). Preferred indications include neoplasms, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer.

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				immunomodulatory factors.	Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
78	НАТБН20	542	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphoca, anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia.
					neutrophilia, psoriasis, suppression of immune reactions to

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					nanspirance organs and ussues, nemopinina, hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
<u>.</u> .					asthma and allergy. An additional preferred indication
					is intection (e.g., an infectious disease as described below under "Infectious Disease").
59	HBAGD86	543	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription via	through the DMEF1 response element are	An additional highly preferred indication is a complication
			DMEF1 response	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			element in adipocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
			and pre-adipocytes	polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to activate the DMEF1	neuropathy, nerve disease and nerve damage (e.g., due to
				response element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
				(such as that containing the GLUT4	stroke, impotence (e.g., due to diabetic neuropathy or
				promoter) and to regulate insulin	blood vessel blockage), seizures, mental confusion,
				production. The DMEF1 response	drowsiness, nonketotic hyperglycemic-hyperosmolar
				element is present in the GLUT4 promoter	coma, cardiovascular disease (e.g., heart disease,
				and binds to MEF2 transcription factor and	atherosclerosis, microvascular disease, hypertension,
				another transcription factor that is required	stroke, and other diseases and disorders as described in the
	-			for insulin regulation of Glut4 expression	"Cardiovascular Disorders" section below), dyslipidemia,
				in skeletal muscle. GLUT4 is the primary	endocrine disorders (as described in the "Endocrine
				insulin-responsive glucose transporter in	Disorders" section below), neuropathy, vision impairment
				fat and muscle tissue. Exemplary assays	(e.g., diabetic retinopathy and blindness), ulcers and
				that may be used or routinely modified to	impaired wound healing, and infection (e.g., infectious
				test for DMEF1 response element activity	diseases and disorders as described in the "Infectious
				(in adipocytes and pre-adipocytes) by	Diseases" section below, especially of the urinary tract and
				polypeptides of the invention (including	tunnel
				antibodies and agonists or antagonists of	contracture). An additional highly preferred
				the invention) include assays disclosed	indication is obesity and/or complications associated with
				inThai, M.V., et al., J Biol Chem,	obesity. Additional highly preferred indications include
				273(23):14285-92 (1998); Mora, S., et al.,	weight loss or alternatively, weight gain. Aditional
				J Biol Chem, 275(21):16323-8 (2000); Liu,	highly preferred indications are complications associated
				M.L., et al., J Biol Chem, 269(45):28514-	with insulin resistance.
				21 (1994); "Identification of a 30-base pair	
				regulatory element and novel DNA	
				binding protein that regulates the human	

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.
GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation culture conditions.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to bind the serum response factor and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in
·	Activation of transcription through serum response element in immune cells (such as T-cells).
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			·	Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below and arther "Infectious Disease")
53	HBAGD86	543	Activation of transcription through STAT6 response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the	A highly preferred indication is allergy. A highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include inflammation and inflammatory disorders (e.g., as described below under "Tmmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms, such as, for example,

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				antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Tmmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and
53	HBAGD86	543	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example,

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include assays disclosed in Berger et al., Gene 66:1-10 (1998); Culten and Malm. Gene 66:1-10 (1998); Culten and Malm. Gene 66:1-10 (1998); Culten and Malm. Methods in Enzymol 216:362-368 (1992); Exhort or et al., Proc Natl Acad Soi USA 85:6342-6346 (1988); Aramburu et al., 50 Cancer. Other preferred indications include benign Henthorn et al., Proc Natl Acad Soi USA 85:6342-6346 (1988); Aramburu et al., 50 Cancer. Other preferred indications include benign Henthorn et al., Proc Natl Acad Soi USA 85:6342-6346 (1988); Aramburu et al., 50 Cancer. Other preferred indications also include anemia, 2011 2012 (1993); Aramburu et al., 50 Cancer. Other acade, 2014 (1993); and 2018 (1993); Braser et al., 50 Cancer of Chem 268(1991); and 2019 (1993); the contents of each of which are herein incorporated by reference in	A highly preferred embodiment of the invention and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production (IgA plays a role in mucosal immunity). IL-6 induces a method for stimulating (e.g., increasing) IL-6 participates in IL-4 induced IgE production (IgA plays a role in mucosal immunity). IL-6 induces cytoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and discase, plasmacytomas, myelomas, and discated below under "Infantion (IgA plays a required) at large variety of cells where the expression level is strongly regulated by expression level is strongly regulated by croutinely modified to assess the ability of preferred indications also include boosting a B cell- A highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 participates in IL-4 induced IgE production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention of the
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			antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by	B cell-mediated immune response. Highly preferred indications include inflammation and inflammatory disorders. Additional highly preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphoma, arthritis, AIDS, granulomatous disease, acute lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia,
			reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
31 HBDAB91	545	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to

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				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
	-			assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
				(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
-				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
32	HBDAB91	546	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic remiopaniy,

described in the "Renal Disorders" section below), diabetic Diseases" section below, especially of the urinary tract and stroke, and other diseases and disorders as described in the diabetic neuropathy), blood vessel blockage, heart disease, Disorders" section below), neuropathy, vision impairment Aditional indication is obesity and/or complications associated with neuropathy, nerve disease and nerve damage (e.g., due to "Cardiovascular Disorders" section below), dyslipidemia, nighly preferred indications are complications associated obesity. Additional highly preferred indications include diabetic nephropathy, kidney disease (e.g., renal failure, impaired wound healing, and infection (e.g., infectious stroke, impotence (e.g., due to diabetic neuropathy or diseases and disorders as described in the "Infectious (e.g., diabetic retinopathy and blindness), ulcers and drowsiness, nonketotic hyperglycemic-hyperosmolar atherosclerosis, microvascular disease, hypertension, endocrine disorders (as described in the "Endocrine nephropathy and/or other diseases and disorders as blood vessel blockage), seizures, mental confusion. An additional highly preferred coma, cardiovascular disease (e.g., heart disease, skin), carpal tunnel syndrome and Dupuytren's weight loss or alternatively, weight gain. with insulin resistance. contracture). line established from cells isolated from an Kim, K.H., et al., FEBS Lett, 377(2):237-9 according to these assays include rat INS-1 insulin secretion. References: Asfari et al. of polypeptides of the invention (including entirety. Pancreatic cells that may be used characteristics typical of native pancreatic cells. INS-1 cells are a semi-adherent cell available (e.g., through the ATCC) and/or insulin antibodies. Insulin secretion from the invention) include assays disclosed in: secretion. For example, insulin secretion modified to test for stimulation of insulin (1995); and, Miraglia S et. al., Journal of antibodies and agonists or antagonists of Ahren, B., et al., Am J Physiol, 277(4 Pt antibodies and agonists or antagonists of polypeptides of the invention (including may be routinely generated. Exemplary proteins/peptides, and disregulation is a Endocrinology, 138(9):3735-40 (1997); (1999), the contents of each of which is key component in diabetes. Exemplary herein incorporated by reference in its pancreatic beta cells is upregulated by beta cells including glucose inducible according to these assays are publicly is measured by FMAT using anti-rat Biomolecular Screening, 4:193-204 assays that may be used or routinely secretion (from pancreatic cells) by the invention) to stimulate insulin 2):R959-66 (1999); Li, M., et al., pancreatic cells that may be used X-ray induced rat transplantable insulinoma. These cells retain glucose and also by certain

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				Endocrinology 1992 130:167.	
33	HBGBC29	547	Protection from	Caspase Apoptosis Rescue. Assays for	A highly preferred embodiment of the invention
			Endothelial Cell	caspase apoptosis rescue are well known in	includes a method for stimulating endothelial cell growth.
			Apoptosis.	the art and may be used or routinely	An alternative highly preferred embodiment of the
				modified to assess the ability of the	invention includes a method for inhibiting endothelial cell
				polypeptides of the invention (including	growth. A highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for stimulating endothelial
				the invention) to inhibit caspase protease-	cell proliferation. An alternative highly preferred
				mediated apoptosis. Exemplary assays for	_
				caspase apoptosis that may be used or	inhibiting endothelial cell proliferation. A highly
				routinely modified to test caspase	preferred embodiment of the invention includes a method
				apoptosis rescue of polypeptides of the	for stimulating endothelial cell growth. An alternative
				invention (including antibodies and	highly preferred embodiment of the invention includes a
				agonists or antagonists of the invention)	method for inhibiting endothelial cell growth. A
				include the assays disclosed in Romeo et	highly preferred embodiment of the invention includes a
				al., Cardiovasc Res 45(3): 788-794 (2000);	method for stimulating apoptosis of endothelial cells. An
				Messmer et al., Br J Pharmacol 127(7):	alternative highly preferred embodiment of the invention
				1633-1640 (1999); and J Atheroscler	includes a method for inhibiting (e.g., decreasing)
				Thromb 3(2): 75-80 (1996); the contents of	apoptosis of endothelial cells. A highly preferred
				each of which are herein incorporated by	embodiment of the invention includes a method for
				reference in its entirety. Endothelial cells	stimulating angiogenisis. An alternative highly preferred
				that may be used according to these assays	embodiment of the invention includes a method for
				are publicly available (e.g., through	inhibiting angiogenesis. A highly preferred
				commercial sources). Exemplary	embodiment of the invention includes a method for
				endothelial cells that may be used	reducing cardiac hypertrophy. An alternative highly
				according to these assays include bovine	preferred embodiment of the invention includes a method
				aortic endothelial cells (bAEC), which are	for inducing cardiac hypertrophy. Highly preferred
				an example of endothelial cells which line	indications include neoplastic diseases (e.g., as described
				blood vessels and are involved in functions	below under "Hyperproliferative Disorders"), and
				that include, but are not limited to,	disorders of the cardiovascular system (e.g., heart disease,
				angiogenesis, vascular permeability,	congestive heart failure, hypertension, aortic stenosis,
				vascular tone, and immune cell	cardiomyopathy, valvular regurgitation, left ventricular
				extravasation.	dysfunction, atherosclerosis and atherosclerotic vascular
					disease, diabetic nephropathy, intracardiac shunt, cardiac
					hypertrophy, myocardial infarction, chronic hemodynamic
		<u> </u>			overload, and/or as described below under
					Cardiovascular Disorders). Inigniy preferred

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angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the	vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications	that stimulate angiogenesis and/or cardiovascularization.	Highly preferred are indications that inhibit angiogenesis	and/or cardiovascularization. Highly preterred indications include antiangiogenic activity to treat solid	retinal	disorders. Highly preferred indications include neoplasms	ngioma	(capillary and cavernous), glomus tumors, telangiectasia,	la,	angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also	; colon,	pancreatic, esophageal, stomach, brain, liver, and urinary		dysproliferative disorders and pre-neoplastic conditions,	, and/or	Highly preferred indications also include	rtension,	itides,	m,	aneurysms, restenosis; venous and lymphatic disorders	such as thrombophlebitis, lymphangitis, and lymphedema;	and other vascular disorders such as peripheral vascular	disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	(e.g., vascular injury such as, injury resulting from balloon	plant	fixation, scarring, ischemia reperfusion injury, rheumatoid	arthritis, cerebrovascular disease, renal diseases such as	Additional highly	ection.
disorders well as di	vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indica	ardiovasc	t inhibit a	Highly preleffed ic activity to treat	tumors, leukemias, and Kaposi's sarcoma, and retinal	ons includ	and cancer, such as, Kaposi's sarcoma, hemangioma	ımors, tel	bacillary angiomatosis, hemangioendothelioma,	a, lympl	red indica	include cancers such as, prostate, breast, lung, colon,	rain, liver,	e benign	eoplastic	such as, for example, hyperplasia, metaplasia, and/or	cations al	arterial disease, such as, atherosclerosis, hypertension,	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	ymphatic	itis, and l	s peripher.	erred indi	ns, and in	resulting	angioplasty, and atheroschlerotic lesions), implant	ion injury	nal disea	s. Add	preferred indications include stroke, graft rejection,
systemic ellitus, as	of the ar Highly or	and/or ca	tions that	ingenic a	posi's sare	indicatio	i's sarcon	glomus tu	nangioen	ericytom	ıly preferi	ostate, br	mach, br	cancer. Preferred indications include benign	and pre-n	rplasia, m	rred indic	heroscler	flammato	maud's ph	ous and ly	lymphang	rs such as	ighly pref	unds, bur	as, injury	lerotic les	a reperfus	lisease, re	acute renal failure, and osteoporosis.	de stroke.
ers (e.g., abetes me	s, such as	iogenesis	are indica	and/or cardiovascularization. indications include antiangiog	s, and Ka	preferred	as, Kapos	ernous),	ıtosis, her	emangiop	ma. High	uch as, pr	ageal, sto	indicatio	isorders a	ple, hype	ghly prefe	uch as, at	isease, in	e and Rey	iosis; ven	hlebitis, 1	r disorde	er. Hi	ich as wo	ury such	atherosch	, ischemia	/ascular d	e, and ost	ons inclu
nic disord	hemselve d/or lymr	ulate ang	referred	ardiovasc	leukemia	s. Highly	er, such	y and cav	angioma /	coma, ha	giosarco	cancers so	ic, esoph	Preferred	ferative d	for exam		disease, s	y artery d	l's disease	ms, rester	thrombop	r vascula	and canc	trauma su	scular inj	sty, and	, scarring	, cerebro	nal failur	d indicati
angiogenic disorders (e.g., systemic disorders that afferessels such as diabetes mellitus, as well as diseases o	vessels t	that stim	Highly F	and/or c	tumors,	disorder	and cano	(capillar	bacillary	angiosar	lymphar	include	pancreat	cancer.	dysproli	such as,	dysplasia.	arterial	coronar	Reynand	aneurysi	such as	and othe	disease,	include	(e.g., va	angiopla	fixation	arthritis	acute re	nreferre
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		ı			disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory diseases, e.g., inflammatory bowel disease
34 HBGNC72	NC72	548	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplastic diseases

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				Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and prenepalastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, mand allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
35	НВНАА05	549	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and

ectious ious y tract and ated with include Sociated	llitus. uplication y, failure, as i), diabetic failore, tr disease, hy or on, olar iion, libed in the lipidemia,
impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia,
impaired wound healing, and infection (e.g., in diseases and disorders as described in the "Infe Diseases" section below, especially of the urina skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferr indication is obesity and/or complications assocobesity. Additional highly preferred indication weight loss or alternatively, weight gain. highly preferred indications are complications with insulin resistance.	indication is eferred indication is eferred indices (e.g., diabe idney disease are diseases a Disorders" see and nerve cod vessel be due to diabe seizures, me hyperglycem isease (e.g., lascalar disease and disorers, section ers." section
impaired wound healing diseases and disorders a Diseases" section below skin), carpal tunnel syn contracture). An a indication is obesity and obesity. Additional hig weight loss or alternativhighly preferred indicat with insulin resistance.	ly preferred vital highly prayer diabetes with diabetes phropathy, k y and/or oth n the "Renal uropathy), blotence (e.g., sl blockage), nonketotic lovascular diseas other diseas cular Disord
impaired wou diseases and Diseases" sec skin), carpal contracture). indication is obesity. Add weight loss o highly prefer with insulin r	A high An addition associated v diabetic nep nephropath described ii neuropathy diabetic neu stroke, imp blood vesse drowsiness, coma, cardia atherosclere stroke, and "Cardiovass
drichsen (1):136-48 octinology, et al., J (17771-9 which is is in its ay be used blicly C) and/or emplary f er at INS-1 terent cell ed from an cible sancreatic cible ssfari et al.	of insulin ay be used he ability (including onists of n secretion i-rat tion from ted by ion is a mplary nely in insulin
sts of the invosed in: Frieborinol, 15(1), et al., Endo 8); Hugl SR, 10;273(28); of each of w by reference cells that missays are pulagh the ATC nerated. Exemply be used ssays include e a semi-adh an cells isolat ansplantable cells retain all of native glucose indueferences: A 2 130:167.	ig secretion of the art and make invention ists or antage mulate insulinable, insulinable, insulinable, insulinable is upregulate certain and disregulates. Exelusted or routination of stimulation of stimulation of the art and the the art a
agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin
agonisti include BN, et (2001); 139(4); Biol Ch (1998), herein i entirety accordi availabl may be pancrea accordi cells. I line esti X-ray ii insulino characte beta cel insulino Endocri	Assays are well or routi of polyj antibod the inve secretio is meas insulin pancrea glucose proteins key con assays t
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	Insulin Secretion
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				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
				(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
				Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
				Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
				865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
				Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
				Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
				Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
				of each of which is herein incorporated by	with insulin resistance.
				reference in its entirety. Pancreatic cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC) and/or may be routinely generated.	
				Exemplary pancreatic cells that may be	
				used according to these assays include	
				HITT15 Cells. HITT15 are an adherent	
				epithelial cell line established from Syrian	
				hamster islet cells transformed with SV40.	
			٠	These cells express glucagon,	
				somatostatin, and glucocorticoid receptors.	
				The cells secrete insulin, which is	
				stimulated by glucose and glucagon and	
				suppressed by somatostatin or	
				glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
36	HBHAA81	550	Production of	IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	invention includes a method for inhibiting the production
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune

macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
 of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
helper cell functions are well known in the	Highly preferred indications include autoimmune disease
art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
inflammatory activities, modulate TH2	indications include inflammation and inflammatory
 helper cell function, and/or mediate	disorders. Additional preferred indications include
humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
 Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
polypeptides of the invention (including	include benign dysproliferative disorders and pre-
antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
 Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
 (1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
 Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
of each of which are herein incorporated	
by reference in its entirety. Human T cells	
that may be used according to these assays	
may be isolated using techniques disclosed	

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				herein or otherwise known in the art.	
				Human T cells are primary human	
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
37	HBIAA59	551	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			•	or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	ou o
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	described below under "Infectious Disease").
				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An

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	that may be used according to these assays	additional highly preferred indication is a complication
	adherent mouse preadipocyte cell line that	disoctated with diabetes (e.g., diabetic remopanity, diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and
		impaired wound healing, infection (e.g., infectious
		diseases and disorders as described in the "Infectious
		Diseases" section below (particularly of the urinary tract
		and skin). An additional highly preferred indication is
		obesity and/or complications associated with obesity.
		Additional highly preferred indications include weight loss
		or alternatively, weight gain. Additional highly
		preferred indications are complications associated with
		insulin resistance. Additional highly preferred
		indications are disorders of the musculoskeletal systems
		hies,
		described herein. Additional highly preferred
		indications include, hypertension, coronary artery disease,
		dyslipidemia, gallstones, osteoarthritis, degenerative
		arthritis, eating disorders, fibrosis, cachexia, and kidney
		diseases or disorders. Preferred indications include
-		neoplasms and cancer, such as, lymphoma, leukemia and
		breast, colon, and kidney cancer. Additional preferred
		indications include melanoma, prostate, lung, pancreatic,
		esophageal, stomach, brain, liver, and urinary cancer.

				Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
38 HBIAC29	552	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, lumbnocytopenia, Hodgkin's disease, acute lymphocytic and anemia (ALL), plasmacytomas, multiple myeloma, anemia, a

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					disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
39 HBI	HBICW51	553	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brant, liver and urinary cancer. Other preferred indications
				polypeptides of the invention (including antibodies and agonists or antagonists of	include benign dysproliferative disorders and pre- neoplastic conditions, such as, for example, hyperplasia,

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metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Bone and Cartilage Diseases, including but not limited to Arthritis, Cartilige repair, Bone Repair, Osteoporosis, and related tumors including chondrosarcomas, chondroblastomas, and chondromas.
the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux in chondrocytes include
	Calcium flux in chondrocytes
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				Inflamm Res, 50(1):19-23 (2001); Schwartz Z, et al., J Bone Miner Res, 6(7):709-718 (1991); Jannotti JP, et al., J Bone Joint Surg Am, 67(1): 113-120 (1985); Sullivan E., et al., Methods Mol Biol 1999; 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include	
40 HBJ/	HBJAB02	554	Upregulation of T cells and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and

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				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
_				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
,				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
41	HBJAC65	555	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neopiastic conditions,

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				cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, eukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and
42	нвлвм12	556	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly

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				a large variety of cells where the	preferred indications include autoimmine diseases (e.g.
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders.Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
43	HBJCR46	557	Regulation of viability	Assays for the regulation of viability and	A highly preferred indication is diabetes mellitus.

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and proliferation of	proliferation of cells in vitro are well-	An additional highly preferred indication is a complication
pancreatic beta cells.	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
	polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
	antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
	the invention) to regulate viability and	neuropathy, nerve disease and nerve damage (e.g., due to
	proliferation of pancreatic beta cells. For	diabetic neuropathy), blood vessel blockage, heart disease,
	example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
	cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
	viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
	quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
	signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
	active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
	used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
	regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
	pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
	invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
	agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
	include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
	BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
	(2001); Huotari MA, et al., Endocrinology,	skin), carpal tunnel syndrome and Dupuytren's
	139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
	Biol Chem 1998 Jul 10;273(28):17771-9	indication is obesity and/or complications associated with
	(1998), the contents of each of which is	cations i
	herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
	entirety. Pancreatic cells that may be used	highly preferred indications are complications associated
	according to these assays are publicly	with insulin resistance.
	available (e.g., through the ATCC) and/or	
	may be routinely generated. Exemplary	
	pancreatic cells that may be used	
	according to these assays include rat INS-1	
	cells. INS-1 cells are a semi-adherent cell	
	line established from cells isolated from an	
	X-ray induced rat transplantable	
	insulinoma. These cells retain	
	characteristics typical of native pancreatic	
	beta cells including glucose inducible	

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: Asfari et al.	a. CTLA-4) A highly preferred embodiment of the invention ivated T cells. Includes a method for activating T cells. An alternative		on method for i							_	in the art and "Cardiovascular Disorders"), Highly preferred indications								that test for under "Hyperproliferative Disorders"). Additionally,	evaluate the highly preferred indications include neoplasms and	- ch						include, for Preferred indications include anemia, pancytopenia,	i in Miraglia leukopenia, thrombocytopenia, Hodgkin's disease, acute	ing 4:193-204 lymphocytic anemia (ALL), plasmacytomas, multiple		6:138-160 granulomatous disease, inflammatory bowel disease,	ol Cell Biol sepsis, neutropenia, neutrophilia, psoriasis, immune	gal et al., Curr reactions to transplanted organs and tissues, hemophilia,
insulin secretion. References: Endocrinology 1992 130:167	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells.	CD152 is a negative regulator of T cell	proliferation. Reduced CD152 expression	has been linked to hyperproliferative and	autoimmune diseases. Overexpression of	CD152 may lead to impaired	immunoresponses. Assays for	immunomodulatory proteins important in	the maintenance of T cell homeostasis and	expressed almost exclusively on CD4+ and	CD8+ T cells are well known in the art and	may be used or routinely modified to	assess the ability of polypeptides of the	invention (including antibodies and	agonists or antagonists of the invention) to	modulate the activation of T cells,	maintain T cell homeostasis, and/or	mediate humoral or cell-mediated	immunity. Exemplary assays that test for	immunomodulatory proteins evaluate the	upregulation of cell surface markers, such	as CD152, and the activation of T cells.	Such assays that may be used or routinely	modified to test immunomodulatory	activity of polypeptides of the invention	(including antibodies and agonists or	antagonists of the invention) include, for	example, the assays disclosed in Miraglia	et al., J Biomolecular Screening 4:193-204	(1999); Rowland et al., "Lymphocytes: a	practical approach" Chapter 6:138-160	(2000); McCoy et al., Immunol Cell Biol	77(1):1-10 (1999); Oostervegal et al., Curr Onin Imminol 11/3>:204-300 (1999); and
	Upregulation of CD152 and activation of T cells																																
	558																																
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indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Il an an an an an are complications associated with insulin resistance.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious
Biol Chem 1998 Jul 10,273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinelly generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen
	Regulation of viability and proliferation of pancreatic beta cells.
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Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for activation B cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating B cells. A highly preferred embodiment of the invention includes a method for activating NK cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting activation of and/or inactivation NK cells. Highly preferred indications include inflammation and inflammatory disorders (e.g., as described below under "Immune Activity"). Preferred indications include blood disorders (e.g., as described below under "Immune
BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	CD69 FMAT. CD69 is an activation marker that is expressed on activated T cells, B cells, and NK cells. CD69 is not expressed on resting T cells, B cells, or NK cells. CD69 has been found to be associated with inflammation. Assays for immunomodulatory proteins expressed in T cells, B cells, and leukocytes are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cellmediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface
	Upregulation of T cells and activation of T cells
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				markers, such as CD69, and the activation	Activity", "Blood-Related Disorders", and/or
				of T cells. Such assays that may be used	"Cardiovascular Disorders"). Highly preferred indications
				or routinely modified to test	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory activity of	systemic lupus erythematosis, multiple sclerosis and/or as
				polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
				antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
				the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
				assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
				Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
				Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
				approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
				Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
				(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
				(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
				Afetra et al., Ann Rheum Dis 52(6):457-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,
				are herein incorporated by reference in its	neutrophilia, psoriasis, suppression of immune reactions to
				entirety. Human T cells that may be used	transplanted organs and tissues, hemophilia,
				according to these assays may be isolated	hypercoagulation, diabetes mellitus, endocarditis,
				using techniques disclosed herein or	meningitis, Lyme Disease, inflammation and
				otherwise known in the art. Human T cells	inflammatory disorders, asthma, and allergies.
				are primary human lymphocytes that	Preferred indications also include neoplastic diseases (e.g.,
				mature in the thymus and express a T Cell	leukemia, lymphoma, and/or as described below under
				receptor and CD3, CD4, or CD8. These	"Hyperproliferative Disorders"). Preferred indications
				cells mediate humoral or cell-mediated	include neoplasms, such as, for example, leukemia,
				immunity and may be preactivated to	lymphoma, and prostate, breast, lung, colon, pancreatic,
				enhance responsiveness to	esophageal, stomach, brain, liver and urinary cancer.
				immunomodulatory factors.	Other preferred indications include benign dysproliferative
					disorders and pre-neoplastic conditions, such as, for
					example, hyperplasia, metaplasia, and/or dysplasia.
47	HBJFK45	561	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkins

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				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
			-	the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
				as the SUPT cell line, that may be used	include anemia, pancytopenia, leukopenia,
	-			according to these assays are publicly	thrombocytopenia, acute lymphocytic anemia (ALL),
				available (e.g., through the ATCC).	plasmacytomas, multiple myeloma, arthritis, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, neutropenia, neutrophilia, psoriasis, suppression of
					immune reactions to transplanted organs and tissues,
					hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
47	HBJFK45	561	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			NFAT response	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
			element in immune	known in the art and may be used or	Disorders"). Highly preferred indications include
			cells (such as natural	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
			killer cells).	polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
				antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),

inmune response. lications include y disorders. An additional nfection (e.g., an infectious ler "Infectious Disease"). eoplastic diseases (e.g., s described below under y). Preferred indications s, such as, for example, tate, breast, lung, colon, th, brain, liver and urinary ions include benign pre-neoplastic conditions, sia, metaplasia, and/or ons also include anemia, mbocytopenia, Hodgkin's mia (ALL), plasmacytomas, mphoma, arthritis, AIDS, matory bowel disease, ia, psoriasis, suppression of ed organs and tissues, diabetes mellitus, Disease, asthma and	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a method for stimulating muscle cell proliferation is
boosting a 1 cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, braait, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a method for stimulating muscle cell proliferation. In a
the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for P13 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polymentides of the invention (including
	Activation of Skeletal Mucle Cell P13 Kinase Signalling Pathway
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antidodies and agonists of antagonists of	stimulated. An atternative nigniy preferred embodiment of
the invention) to promote or inhibit	the invention includes a method for inhibiting muscle cell
 glucose metabolism and cell survival.	proliferation. In a specific embodiment, skeletal muscle
Exemplary assays for PI3 kinase activity	cell proliferation is inhibited. A preferred embodiment
that may be used or routinely modified to	of the invention includes a method for stimulating muscle
test PI3 kinase-induced activity of	cell differentiation. In a specific embodiment, skeletal
 polypeptides of the invention (including	muscle cell differentiation is stimulated. An alternative
antibodies and agonists or antagonists of	highly preferred embodiment of the invention includes a
the invention) include assays disclosed in	method for inhibiting muscle cell differentiation. In a
Forrer et al., Biol Chem 379(8-9):1101-	specific embodiment, skeletal muscle cell differentiation is
1110 (1998); Nikoulina et al., Diabetes	inhibited. Highly preferred indications include disorders
49(2):263-271 (2000); and Schreyer et al.,	of the musculoskeletal system. Preferred indications
Diabetes 48(8):1662-1666 (1999), the	include neoplastic diseases (e.g., as described below under
contents of each of which are herein	"Hyperproliferative Disorders"), endocrine disorders (e.g.,
 incorporated by reference in its entirety.	as described below under "Endocrine Disorders"), neural
Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
available (e.g., through the ATCC).	described below under "Immune Activity",
Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
cells. L6 is an adherent rat myoblast cell	under "Immune Activity"), and infection (e.g., as
line, isolated from primary cultures of rat	described below under "Infectious Disease"). A
thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus. An
multinucleated myotubes and striated	additional highly preferred indication is a complication
fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
	diabetic nephropathy, kidney disease (e.g., renal failure,
	nephropathy and/or other diseases and disorders as
	described in the "Renal Disorders" section below), diabetic
	neuropathy, nerve disease and nerve damage (e.g, due to
	diabetic neuropathy), blood vessel blockage, heart disease,
	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,

					endocrine disorders (as described in the "Endocrine
					Disorders" section below), neuropathy, vision impairment
					(e.g., diabetic retinopathy and blindness), ulcers and
					impaired wound healing, infections (e.g., infectious
					diseases and disorders as described in the "Infectious
			-		Diseases" section below, especially of the urinary tract and
					uun
					contracture). An additional highly preferred indication
					is obesity and/or complications associated with obesity.
					Additional nightly preferred indications include weight loss or alternatively, weight gain.
					nlicati
					insulin resistance Additional highly preferred
					orders o
					including myopathies, muscular dystrophy, and/or as
					described herein. Additional highly preferred
					indications include: myopathy, atrophy, congestive heart
					failure, cachexia, myxomas, fibromas, congenital
					cardiovascular abnormalities, heart disease, cardiac arrest,
					heart valve disease, and vascular disease. Highly
					preferred indications include neoplasms and cancer, such
					as, rhabdomyoma, rhabdosarcoma, stomach, esophageal,
					prostate, and urinary cancer. Preferred indications also
					include breast, lung, colon, pancreatic, brain, and liver
					cancer. Other preferred indications include benign
	· .				dysproliferative disorders and pre-neoplastic conditions,
					such as, hyperplasia, metaplasia, and/or dysplasia.
49	HBJKD16	563	Production of IL-6	L-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as

differentiation factor proteins produced by	described below under "Infections Disease") Highly
a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
or routinely modified to assess the ability	preferred indications also include boosting a B cell-
of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
the invention) to mediate	indications include inflammation and inflammatory
immunomodulation and differentiation and	disorders. Additional highly preferred indications include
modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
differentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
reference in its entirety. Human dendritic	Ħ
cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
disclosed herein or otherwise known in the	described below under "Infectious Disease").
art. Human dendritic cells are antigen	
presenting cells in suspension culture,	
which, when activated by antigen and/or	
cytokines, initiate and upregulate T cell	
proliferation and functional activities.	

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A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory howel disease.	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and asonists or antagonists of the invention) to	mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of nolynentides of the	invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the
Production of · MIP1alpha		
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HBJKD16		
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				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
49	HBJKD16	563	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	tunne
				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred
according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through
	Activation of transcription through serum response element in immune cells (such as T-cells).
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				the ATCC). Exemplary mouse 1 cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below media or the control of the control o
51	HBMBX01	565	Upregulation of T cells and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity," "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,

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				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
			-	(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
52	HBMTM11	995	Protection from	Caspase Apoptosis Rescue. Assays for	A highly preferred embodiment of the invention
			Endothelial Cell	caspase apoptosis rescue are well known in	includes a method for stimulating endothelial cell growth.
			Apoptosis.	the art and may be used or routinely	An alternative highly preferred embodiment of the
				modified to assess the ability of the	invention includes a method for inhibiting endothelial cell
				polypeptides of the invention (including	growth. A highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for stimulating endothelial
				the invention) to inhibit caspase protease-	cell proliferation. An alternative highly preferred
				mediated apoptosis. Exemplary assays for	шe
				caspase apoptosis that may be used or	inhibiting endothelial cell proliferation. A highly
				routinely modified to test caspase	preferred embodiment of the invention includes a method

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invention (including antibodies and	highly preferred embodiment of the invention includes a
agonists or antagonists of the invention)	method for inhibiting endothelial cell growth. A
include the assays disclosed in Romeo et	highly preferred embodiment of the invention includes a
al., Cardiovasc Res 45(3): 788-794 (2000);	method for stimulating apoptosis of endothelial cells. An
Messmer et al., Br J Pharmacol 127(7):	alternative highly preferred embodiment of the invention
1633-1640 (1999); and J Atheroscler	•
Thromb 3(2): 75-80 (1996); the contents of	apoptosis of endothelial cells. A highly preferred
 each of which are herein incorporated by	embodiment of the invention includes a method for
reference in its entirety. Endothelial cells	stimulating angiogenisis. An alternative highly preferred
that may be used according to these assays	embodiment of the invention includes a method for
are publicly available (e.g., through	inhibiting angiogenesis. A highly preferred
commercial sources). Exemplary	embodiment of the invention includes a method for
endothelial cells that may be used	reducing cardiac hypertrophy. An alternative highly
according to these assays include bovine	preferred embodiment of the invention includes a method
aortic endothelial cells (bAEC), which are	for inducing cardiac hypertrophy. Highly preferred
an example of endothelial cells which line	indications include neoplastic diseases (e.g., as described
blood vessels and are involved in functions	below under "Hyperproliferative Disorders"), and
that include, but are not limited to,	disorders of the cardiovascular system (e.g., heart disease,
angiogenesis, vascular permeability,	congestive heart failure, hypertension, aortic stenosis,
vascular tone, and immune cell	cardiomyopathy, valvular regurgitation, left ventricular
extravasation.	dysfunction, atherosclerosis and atherosclerotic vascular
	disease, diabetic nephropathy, intracardiac shunt, cardiac
	hypertrophy, myocardial infarction, chronic hemodynamic
	overload, and/or as described below under
	"Cardiovascular Disorders"). Highly preferred
	indications include cardiovascular, endothelial and/or
	angiogenic disorders (e.g., systemic disorders that affect
	vessels such as diabetes mellitus, as well as diseases of the
	vessels themselves, such as of the arteries, capillaries,
	veins and/or lymphatics). Highly preferred are indications
	that stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms

		below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred embodiment of mucosal inflication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below) and inflammatory disorders. Additional highly preferred indications include asthma and allergy. Highly preferred indications include asthma and allergy. Highly preferred indications include heoplastic diseases (e.g., myeloma, plasmacytoma, plasmacytoma, leukemia, lymphoma, melanoma, and or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
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HBMTY48 568 Act Mu Sig	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway	J Biomolecular Screening 4:193- 204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Kinase assay. Kinase assay, for example an GSK-3 kinase assay, for P13 kinase signal transduction that regulate glucose metabolism and cell survivial are well- known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for increasing muscle cell survival. A preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is inhibited. A preferred embodiment of the invention includes a method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation. In a specific embodiment of the invention includes a method for inhibiting muscle cell differentiation. In a specific embodiment of the invention includes a method for inhibiting muscle cell differentiation. In a specific embodiment of the invention includes a method for inhibiting muscle cell differentiation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is stimulated. In a specific embodiment, skeletal muscle cell differentiation is stimulated. In a specific embodiment, skeletal muscle cell differentiation is stimulated. In a specific embodiment, skeletal muscle cell differentiation is stimulated.
		1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incompared by reference in its entirety	inhibited. Highly preferred indications include disorders of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), endocrine disorders (e.g., as described below under "Endocrine Disorders") neural

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Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
available (e.g., through the ATCC).	described below under "Immune Activity",
Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
cells. L6 is an adherent rat myoblast cell	, as
line, isolated from primary cultures of rat	A
thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus. An
multinucleated myotubes and striated	additional highly preferred indication is a complication
fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
	diabetic nephropathy, kidney disease (e.g., renal failure,
	nephropathy and/or other diseases and disorders as
	described in the "Renal Disorders" section below), diabetic
	neuropathy, nerve disease and nerve damage (e.g, due to
	diabetic neuropathy), blood vessel blockage, heart disease,
	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infections (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below, especially of the urinary tract and
	skin), carpal tunnel syndrome and Dupuytren's
	contracture). An additional highly preferred indication
	is obesity and/or complications associated with obesity.
	ndicatic
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additonal highly preferred
	indications are disorders of the musculoskeletal system
	including myopathies, muscular dystrophy, and/or as

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				described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as hymeralasia and/or dysplasia
55 HBMUH74	269	Regulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesis. Malic enzyme is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors. Exemplary assays that may be used or routinely modified to test for regulation of transcription of Malic Enzyme (in adipoocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Streeper, R.S., et al., Mol Endocrinol, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious diseases and disorders as described in the "Infectious diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with

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weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include asthma and allergy. Highly preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described
I., et al., J Biol Chem, 274(25):17997-8004 (1999); Ijpenberg, A., et al., J Biol Chem, 272(32):20108-20117 (1997); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays includes the H4IIE rat liver hepatoma cell line.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the
	Production of IL-6
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	-			production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"), Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
	<u>-</u>			diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additonal preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
57 HBNAX40	X40 571	.1	Activation of	Assays for the activation of transcription	A highly preferred indication includes allergy. A
			transcription through	through the GATA3 response element are	highly preferred indication includes asthma. A highly
			GATA-3 response	well-known in the art and may be used or	preferred indication includes rhinitis. Additional highly
			element in immune	routinely modified to assess the ability of	preferred indications include infection (e.g., an infectious
			cells (such as T-cells).	polypeptides of the invention (including	disease as described below under "Infectious Disease"),
				antibodies and agonists or antagonists of	and inflammation and inflammatory disorders.
				the invention) to regulate GATA3	Preferred indications include blood disorders (e.g., as
				transcription factors and modulate	described below under "Immune Activity", "Blood-
				expression of genes important for Th2	Related Disorders", and/or "Cardiovascular Disorders").
				immune response development.	Preferred indications include autoimmune diseases (e.g.,
				Exemplary assays for transcription through	rheumatoid arthritis, systemic lupus erythematosis,
				the GATA3 response element that may be	multiple sclerosis and/or as described below) and
				used or routinely modified to test GATA3-	immunodeficiencies (e.g., as described below).

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				response element activity of polypeptides	Preferred indications include neoplastic diseases (e.g.,
				of the invention (including antibodies and	leukemia, lymphoma, melanoma, and/or as described
				agonists or antagonists of the invention)	below under "Hyperproliferative Disorders"). Preferred
				include assays disclosed in Berger et al.,	indications include neoplasms and cancer, such as, for
				Gene 66:1-10 (1998); Cullen and Malm,	example, leukemia, lymphoma, melanoma, and prostate,
				Methods in Enzymol 216:362-368 (1992);	breast, lung, colon, pancreatic, esophageal, stomach,
				Henthorn et al., Proc Natl Acad Sci USA	brain, liver and urinary cancer. Other preferred indications
				85:6342-6346 (1988); Flavell et al., Cold	include benign dysproliferative disorders and pre-
				Spring Harb Symp Quant Biol 64:563-571	neoplastic conditions, such as, for example, hyperplasia,
•				(1999); Rodriguez-Palmero et al., Eur J	metaplasia, and/or dysplasia. Preferred indications
				Immunol 29(12):3914-3924 (1999); Zheng	include anemia, pancytopenia, leukopenia,
				and Flavell, Cell 89(4):587-596 (1997);	thrombocytopenia, leukemias, Hodgkin's disease, acute
				and Henderson et al., Mol Cell Biol	lymphocytic anemia (ALL), plasmacytomas, multiple
				14(6):4286-4294 (1994), the contents of	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				each of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
				reference in its entirety. T cells that may	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				be used according to these assays are	immune reactions to transplanted organs and tissues,
				publicly available (e.g., through the	hemophilia, hypercoagulation, diabetes mellitus,
				ATCC). Exemplary mouse T cells that	endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays	
				include the HT2 cell line, which is a	
				suspension culture of IL-2 dependent T	
				cells that also respond to IL-4.	
58	HBNBJ76	572	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
	_			cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described

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				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
,				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
		,		may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
58	HBNBJ76	572	Production of RANTES	RANTES FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that induce	includes a method for stimulating RANTES production.
				chemotaxis of T cells, monocytes, and	An alternative highly preferred embodiment of the
				eosinophils are well known in the art and	invention includes a method for inhibiting (e.g., reducing)
				may be used or routinely modified to	RANTES production. A highly preferred indication is
				assess the ability of polypeptides of the	infection (e.g., an infectious disease as described below
				invention (including antibodies and	under "Infectious Disease"). A most highly preferred
				agonists or antagonists of the invention) to	indication includes AIDS and/or the prevention or
				mediate immunomodulation, induce	reduction of HIV infection. Additional highly preferred
				chemotaxis, and/or mediate humoral or	indication includes immune disorders, for example,
				cell-mediated immunity. Exemplary	inflammation and inflammatory disorders. Preferred
				assays that test for immunomodulatory	indications include blood disorders (e.g., as described
				proteins evaluate the production of	below under "Immune Activity", "Blood-Related
				cytokines, such as RANTES, and the	Disorders", and/or "Cardiovascular Disorders"). Highly
				induction of chemotactic responses in	preferred indications include autoimmune diseases (e.g.,

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			immune cells. Such assays that may be	rheumatoid arthritis, systemic lupus erythematosis,
			used or routinely modified to test	multiple sclerosis and/or as described below) and
-			immunomodulatory activity of	immunodeficiencies (e.g., as described below).
			polypeptides of the invention (including	Preferred indications also include anemia, pancytopenia,
			antibodies and agonists or antagonists of	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			the invention) include the assays disclosed	lymphocytic anemia (ALL), plasmacytomas, multiple
			in Miraglia et al., J Biomolecular	myeloma, Burkitt's lymphoma, arthritis, asthma,
			Screening 4:193-204 (1999); Rowland et	granulomatous disease, inflammatory bowel disease,
			al., "Lymphocytes: a practical approach"	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
_			Chapter 6:138-160 (2000): Cocchi et al.,	immune reactions to transplanted organs and tissues,
			Science 270(5243):1811-1815 (1995); and	hemophilia, hypercoagulation, diabetes mellitus,
			Robinson et al., Clin Exp Immunol	endocarditis, meningitis, Lyme Disease, asthma, and
			101(3):398-407 (1995), the contents of	allergy. Highly preferred indications also include
			each of which are herein incorporated by	neoplastic diseases (e.g., leukemia, lymphoma, and/or as
-			reference in its entirety. Human immune	described below under "Hyperproliferative Disorders").
			cells that may be used according to these	Highly preferred indications include neoplasms, such as,
•			assays may be isolated using techniques	for example, leukemia, lymphoma, prostate, breast, lung,
			disclosed herein or otherwise known in the	colon, pancreatic, esophageal, stomach, brain, liver, and
			art.	urinary cancer. Other preferred indications include benign
				dysproliferative disorders and pre-neoplastic conditions,
				such as, for example, hyperplasia, metaplasia, and/or
\dashv				dysplasia.
59 HBQAB79	573	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
		secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
		pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
			of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
			antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
			the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
			secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
			is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
			insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
			pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
			glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
	_		proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
			key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
			assays that may be used or routinely	stroke, and other diseases and disorders as described in the
			modified to test for sumulation of insulin	Cardiovascular Disorders section below), dyslipidemia,

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endocrine disorders (as described in the "Endocrine of Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance. NS-1 Cell m an an action are complications associated with a an an are actions.	hichaes a method for stimulating natural killer cell includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include incoplastic diseases (e.g., as described below under
secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1995), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992, 130:167.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be
	Activation of Natural Killer Cell ERK Signaling Pathway.
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kinase-induced activity of polypepides of describe theo under "fineders"), loood disorders (e.g. as a genitis or antigonic nitrol from the says disclosed in Forre et al. Biol Chem 379(4-9);110-1110 (1998), Kyriskis JM, Biochem Soc Symp professore and escribed below under "fineders (e.g., as described ed. (1998); Kyriskis JM, Biochem Soc Symp professore in incitations include blood disorders (e.g., as described ed. (1998); the contents of each of which are pelow under "finediors (e.g., as described below under "finediors (e.g., as described below under "finediors (e.g., as described ed. (1998); the contents of each of which are pelow under "finediors (e.g., as described ed. (1998); the contents of each of which are pelow under "finediors (e.g., as described ed. (1998); the contents of each of which are pelow under "finediors (e.g., as described below) and entirely. Mural killer cell into may be under a content of these assays are public of these assays include the content of the pelow in the content of these assays include the content of strain and the content of the conte
Activation of transcription through serum response element in immune cells (such as T-cells).
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_				growth Exemplary assays for	systemic lupus erythematosis. Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
HBX	HBXCM66	576	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			NFAT response in	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
			immune cells (such as	known in the art and may be used or	Disorders"). Highly preferred indications include
			T-cells).	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
			-	polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described

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		-		antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),
				the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
				transcription factors and modulate	suppressing a T cell-mediated immune response.
				expression of genes involved in	Additional highly preferred indications include
				immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
				assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
				response element that may be used or	disease as described below under "Infectious Disease").
				routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.
				ATCC). Exemplary human T cells that	
				may be used according to these assays	
		•		include the JURKAT cell line, which is a	
				suspension culture of leukemia cells that	
				produce IL-2 when stimulated.	
63	HBXCX15	577	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription via	through the DMEF1 response element are	An additional highly preferred indication is a complication
			DMEF1 response	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			element in adipocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
			and pre-adipocytes	polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic

the invention) to activate the DMFF1	neuronathy nerve disease and nerve damage (e.g., due to
response element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease.
 (such as that containing the GLUT4	stroke, impotence (e.g., due to diabetic neuropathy or
promoter) and to regulate insulin	blood vessel blockage), seizures, mental confusion,
production. The DMEF1 response	drowsiness, nonketotic hyperglycemic-hyperosmolar
element is present in the GLUT4 promoter	coma, cardiovascular disease (e.g., heart disease,
and binds to MEF2 transcription factor and	atherosclerosis, microvascular disease, hypertension,
another transcription factor that is required	stroke, and other diseases and disorders as described in the
for insulin regulation of Glut4 expression	"Cardiovascular Disorders" section below), dyslipidemia,
in skeletal muscle. GLUT4 is the primary	endocrine disorders (as described in the "Endocrine
insulin-responsive glucose transporter in	Disorders" section below), neuropathy, vision impairment
fat and muscle tissue. Exemplary assays	(e.g., diabetic retinopathy and blindness), ulcers and
that may be used or routinely modified to	impaired wound healing, and infection (e.g., infectious
test for DMEF1 response element activity	diseases and disorders as described in the "Infectious
(in adipocytes and pre-adipocytes) by	Diseases" section below, especially of the urinary tract and
polypeptides of the invention (including	skin), carpal tunnel syndrome and Dupuytren's
antibodies and agonists or antagonists of	contracture). An additional highly preferred
the invention) include assays disclosed	indication is obesity and/or complications associated with
inThai, M.V., et al., J Biol Chem,	obesity. Additional highly preferred indications include
273(23):14285-92 (1998); Mora, S., et al.,	weight loss or alternatively, weight gain. Aditional
J Biol Chem, 275(21):16323-8 (2000); Liu,	highly preferred indications are complications associated
M.L., et al., J Biol Chem, 269(45):28514-	with insulin resistance.
21 (1994); "Identification of a 30-base pair	
regulatory element and novel DNA	
binding protein that regulates the human	
GLUT4 promoter in transgenic mice", J	
Biol Chem. 2000 Aug 4;275(31):23666-	
73; Berger, et al., Gene 66:1-10 (1988);	
and, Cullen, B., et al., Methods in	
Enzymol. 216:362–368 (1992), the	
contents of each of which is herein	
incorporated by reference in its entirety.	
Adipocytes and pre-adipocytes that may be	
used according to these assays are publicly	
available (e.g., through the ATCC) and/or	
may be routinely generated. Exemplary	
cells that may be used according to these	

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				assays include the mouse 3T3-L1 cell line	
				which is an adherent mouse preadipocyte	
				cell line. Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3 fibroblasts	
				developed through clonal isolation. These	
				cells undergo a pre-adipocyte to adipose-	
				like conversion under appropriate	
				differentiation culture conditions.	
63 HI	HBXCX15	577	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to bind the	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factor and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
•••				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
-				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
, .				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	Ξ
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
_				AICC). Exemplary human 1 cells, such	indications include anemia, pancytopenia, leukopenia,

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HBXCX15	277	Activation of transcription through STAT6 response element in immune cells (such as natural killer cells).	as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC). Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-	asmacytomas ma, Hodgkin's asmacytomas ma, arthritis, ttory bowel diasis, supprens and tissue; diabetes me Disease, car. V. An add an infectious Disease."). Tred indication is an indication is an indication is an indication is corders. Oisorders. Orders. orders
			368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem	and/or dysplasia. anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs

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				275(38):29331-29337 (2000), the contents	and tissues, hemophilia, hypercoagulation, diabetes
				of each of which are herein incorporated	mellitus, endocarditis, meningitis, and Lyme Disease.
				by reference in its entirety. T cells that	Additional preferred indications include infection (e.g., an
••				may be used according to these assays are	infections disease as described below under "Infectious
				publicly available (e.g., through the	Disease").
				ATCC). Exemplary rat natural killer cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC).	2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
H 69	HBXCX15	577	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
		•	GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	onal
				entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
				as the SOF1 cell line, that may be used	Illetiuue aiteinia, paireytopeina, teunopeina,

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			according to these assays are publicly available (e.g., through the ATCC).	thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
63 HBXCX15	277	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yessen et al. I Biol Chem 268(19):14285.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infectious Disease"). Preferred indication is infectious Diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, pranulomatous disease, inflammatory bowel disease.
			14293 (1993), the contents of each of which are herein incorporated by reference	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,

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in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may the unvention of properties of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the used or routinely modified to assess the antagonists of the invention) to regulate expression of genes involved in growth and upregulate the function of growth related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the modulate sand Mahm, Methods in Enzymol 216:362- and Methods in Enzymol 2
in its entirety. according to the available (e.g., Exemplary hused according NK-YT cell likiller cell line activity.	Activation of transcription through the Se serum response element in immune cells (such as natural killer cells). (including antiant antagonists of serum respons expression of and upregulate related genes? Exemplary ass the SRE that remodified to te polypeptides of antibodies and the invention) Berger et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA) Benson et al., (and Malm, Ma 368 (1992); HA Acad Sci USA)
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thro aner Bur dise neu tran hyp mer asth is ir	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for simulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for simulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune Activity, neural disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Immune Activity"), neural
used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may
	Activation of Adipocyte ERK Signaling Pathway
	578
	HCDCY76
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preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney

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				breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
64 HCDCY76	578	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for simulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular sinease, diabetic nephronathy, intracardiac shunt, cardiac

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hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels as diabetes mellitus, as well as diseases of the vessels	themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as
(bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immine cell extravasation	

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acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g.,
	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
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					pancreatic, esophageal, stomach, brain, liver, and urinary
					cancer. Preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
-					dysplasia. Highly preferred indications also include
					arterial disease, such as, atherosclerosis, hypertension,
					coronary artery disease, inflammatory vasculitides,
					Reynaud's disease and Reynaud's phenomenom,
					aneurysms, restenosis; venous and lymphatic disorders
					such as thrombophlebitis, lymphangitis, and lymphedema;
					and other vascular disorders such as peripheral vascular
					disease, and cancer. Highly preferred indications also
					include trauma such as wounds, burns, and injured tissue
					(e.g., vascular injury such as, injury resulting from balloon
-					angioplasty, and atheroschlerotic lesions), implant
					fixation, scarring, ischemia reperfusion injury, rheumatoid
					arthritis, cerebrovascular disease, renal diseases such as
<u> </u>					acute renal failure, and osteoporosis. Additional highly
					preferred indications include stroke, graft rejection,
					diabetic or other retinopathies, thrombotic and coagulative
					disorders, vascularitis, lymph angiogenesis, sexual
					disorders, age-related macular degeneration, and treatment
-					/prevention of endometriosis and related conditions.
					Additional highly preferred indications include fibromas,
					heart disease, cardiac arrest, heart valve disease, and
					vascular disease. Preferred indications include blood
					disorders (e.g., as described below under "Immune
•					Activity", "Blood-Related Disorders", and/or
					"Cardiovascular Disorders"). Preferred indications include
					autoimmune diseases (e.g., rheumatoid arthritis, systemic
					lupus erythematosis, multiple sclerosis and/or as described
					below) and immunodeficiencies (e.g., as described below).
					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
					and Crohn's disease), and pain management.
66 HCE1G78	G78	580	Endothelial Cell	Caspase Apoptosis. Assays for caspase	A highly preferred embodiment of the invention

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	Apoptosis	apoptosis are well known in the art and	includes a method for stimulating endothelial cell growth.
		may be used or routinely modified to	An alternative highly preferred embodiment of the
		assess the ability of polypeptides of the	invention includes a method for inhibiting endothelial cell
		invention (including antibodies and	growth. A highly preferred embodiment of the
		agonists or antagonists of the invention) to	invention includes a method for stimulating endothelial
		promote caspase protease-mediated	cell proliferation. An alternative highly preferred
		apoptosis. Induction of apoptosis in	meth
		endothelial cells supporting the vasculature	inhibiting endothelial cell proliferation. A highly
		of tumors is associated with tumor	preferred embodiment of the invention includes a method
		regression due to loss of tumor blood	for stimulating apoptosis of endothelial cells. An
		supply. Exemplary assays for caspase	alternative highly preferred embodiment of the invention
		apoptosis that may be used or routinely	ıg (e.g
		modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred
		of polypeptides of the invention (including	embodiment of the invention includes a method for
		antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred
		the invention) include the assays disclosed	embodiment of the invention includes a method for
		in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred
		(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for
		218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
		Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method
		the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred
		incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described
		Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and
		according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
		available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
-		sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
		may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
		include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
		(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
		endothelial cells which line blood vessels	overload, and/or as described below under
		and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
		but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
		vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
		immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
			themselves, such as of the arteries, capillaries, veins and/or
			lymphatics). Highly preterred are indications that
			Stilliulate aligiogenesis alimoi calulo assulatization.

				Highly preferred are indications that inhibit angiogenesis
				and/or cardiovascularization. Highly preferred
				indications include antiangiogenic activity to treat solid
				tumors, leukemias, and Kaposi's sarcoma, and retinal
				disorders. Highly preferred indications include neoplasms
				and cancer, such as, Kaposi's sarcoma, hemangioma
				(capillary and cavernous), glomus tumors, telangiectasia,
				bacillary angiomatosis, hemangioendothelioma,
				angiosarcoma, haemangiopericytoma, lymphangioma,
				lymphangiosarcoma. Highly preferred indications also
			•	include cancers such as, prostate, breast, lung, colon,
				pancreatic, esophageal, stomach, brain, liver, and urinary
				cancer. Preferred indications include benign
				dysproliferative disorders and pre-neoplastic conditions,
				such as, for example, hyperplasia, metaplasia, and/or
				dysplasia. Highly preferred indications also include
	-			arterial disease, such as, atherosclerosis, hypertension,
				coronary artery disease, inflammatory vasculitides,
				Reynaud's disease and Reynaud's phenomenom,
				aneurysms, restenosis; venous and lymphatic disorders
				such as thrombophlebitis, lymphangitis, and lymphedema;
	-			and other vascular disorders such as peripheral vascular
				disease, and cancer. Highly preferred indications also
				include trauma such as wounds, burns, and injured tissue
				(e.g., vascular injury such as, injury resulting from balloon
				angioplasty, and atheroschlerotic lesions), implant
				fixation, scarring, ischemia reperfusion injury, rheumatoid
				arthritis, cerebrovascular disease, renal diseases such as
				acute renal failure, and osteoporosis. Additional highly
				preferred indications include stroke, graft rejection,
				diabetic or other retinopathies, thrombotic and coagulative
				disorders, vascularitis, lymph angiogenesis, sexual
				disorders, age-related macular degeneration, and treatment
				/prevention of endometriosis and related conditions.
				Additional highly preferred indications include fibromas,
				heart disease, cardiac arrest, heart valve disease, and
	:	-		vascular disease. Preferred indications include blood

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					disorders (e.g., as described below under "Immune Activity" "Rlood-Related Disorders" and/or
					"Cardiovascular Disorders"). Preferred indications include
					autoimmune diseases (e.g., rheumatoid arthritis, systemic
					lupus erythematosis, multiple sclerosis and/or as described
					below) and immunodeficiencies (e.g., as described below).
					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
					and Crohn's disease), and pain management.
E2 HCE	HCE2H52	581	Upregulation of CD71	CD71 FMAT. CD71 is the transferrin	A highly preferred embodiment of the invention
			and activation of T cells	receptor. Transferrin is a major iron	includes a method for stimulating T cell proliferation. An
				carrying protein that is essential for cell	alternative highly preferred embodiment of the invention
				proliferation. CD71 is expressed	includes a method for inhibiting T cell proliferation.
				predominantly on cells that are actively	Preferred indications include blood disorders (e.g., as
				proliferating. Assays for	described below under "Immune Activity", "Blood-
				immunomodulatory proteins expressed on	Related Disorders", and/or "Cardiovascular Disorders"),
				activated T cells, B cells, and most	and infection (e.g., as described below under "Infectious
				proliferating cells are well known in the art	Disease"). Highly preferred indications include
				and may be used or routinely modified to	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				assess the ability of polypeptides of the	lupus erythematosis, multiple sclerosis and/or as described
				invention (including antibodies and	below), immunodeficiencies (e.g., as described below),
		•		agonists or antagonists of the invention) to	boosting a T cell-mediated immune response, and
				modulate the activation of T cells, and/or	suppressing a T cell-mediated immune response.
				mediate humoral or cell-mediated	Additional highly preferred indications include
				immunity. Exemplary assays that test for	inflammation and inflammatory disorders. Additional
				immunomodulatory proteins evaluate the	highly preferred indications include infection. Preferred
				upregulation of cell surface markers, such	indications include neoplastic diseases (e.g., leukemia,
				as CD71, and the activation of T cells.	lymphoma, and/or as described below under
				Such assays that may be used or routinely	"Hyperproliferative Disorders"). Preferred indications
				modified to test immunomodulatory	include neoplasms and cancers, such as, for example,
				activity of polypeptides of the invention	leukemia, lymphoma, melanoma, and prostate, breast,
				(including antibodies and agonists or	lung, colon, pancreatic, esophageal, stomach, brain, liver
				antagonists of the invention) include, for	and urinary cancer. Other preferred indications include
				example, the assays disclosed in Miraglia	benign dysproliferative disorders and pre-neoplastic
				et al., J Biomolecular Screening 4:193-204	conditions, such as, for example, hyperplasia, metaplasia,
				(1999); Rowland et al., "Lymphocytes: a	and/or dysplasia. Preferred indications include anemia,

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pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hmunne Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Infectious Diseases"). Preferred indications include blood disorders (e.g., as described below under "Infectious Diseases"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
practical approach." Chapter 6:138-160 (2000); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are
	Activation of Natural Killer Cell ERK Signaling Pathway.
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	·			herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have cytolytic and cytotoxic activity) or primary NK cells.	multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications as, kidney, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, urinary cancer, lymphoma and leukemias. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and
69	HCE5F78	583	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,

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				Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below inder "Inferrious Disease")
07	HCEDR26	584	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment

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(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin L.S, et al., Endocrinology, 136(10):4589-601 (1995);Mogami H, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cells in established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues
	Regulation of apoptosis of immune cells (such as mast cells).
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ion toted n ase. may st cell r r ptosis he 31, 513, 5113 p 52 al., 53 that 5 s are mune mune hese HMC	to method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,
throughout the body, and their activation via immunoglobulin E-antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in
• ·	Activation of transcription through serum response element in immune cells (such as T-cells).
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				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
	·			include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
	·			Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
		-d40			Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
	1			C Company of the Comp	under "Infectious Disease").
72	HCEEQ25	286	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, I cells, tibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	Stimulating (e.g., increasing) INF alpha production.
				Cytotoxic criecus on a variety of cens are	riginy prefered mulcanons include brood disorders (e.g.,

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routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
 antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
proteins evaluate the production of	Additional highly preferred indications include
cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
alpha (TNFa), and the induction or	œ.
inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
routinely modified to test	leukemia, lymphoma, and/or as described below under
immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
 al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
 in suspension culture, which, when	Disease").
activated by antigen and/or cytokines,	
initiate and upregulate T cell proliferation	

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				and functional activities.	
73	HCEEU18	587	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
	-			agonists or antagonists of the invention) to	s a
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	
		· · · · ·		ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
				that may be used according to these assays	additional highly preferred indication is a complication
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
				adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
				is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
				cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
				and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
				TIKE CONVENSION UNGER APPROPRIATE	diadeuc lieuropatily), diodu vessei diockage, licali discase,

	differentiation conditions known in the att.	stroke, impotence (e.g., due to diagetic neuropaniy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious Diseases as ection below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications associated with insulin resistance. Additional highly preferred indications as include weight loss or alternatively, weight gain. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or
HCEEU18 587 Activation of transcription through	Assays for the activation of transcription through the Serum Response Element	aysplasta. A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha

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production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to	transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	
serum response element in immune cells (such as T-cells).	

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					under "Infections Disease")
1	110000000	002		п н н н н н н н н н н н н н н н н н н н	A 1 . 1.1
4	HCEF282	288	Production of 1L-6	IL-6 FMA1. IL-6 is produced by I cells	A nigniy prefered embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000), and veniassentet al., J infilliand	IIIIIaiiiiiaioi y oowel disease, sepsis, ilediiopeilia,

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				158:2919-2925 (1997), the contents of each of which are herein incorporated by	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these assays may be isolated using techniques	meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infections disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
75	HCEGX05	589	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
) 	ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
		-		and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	o uoi
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity

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	be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
	publicly available (e.g., through the	
	ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
	that may be used according to these assays	additional highly preferred indication is a complication
	include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and
		impaired wound healing, infection (e.g., infectious
		diseases and disorders as described in the "Infectious
		Diseases" section below (particularly of the urinary tract
		and skin). An additional highly preferred indication is
		obesity and/or complications associated with obesity.
		Additional highly preferred indications include weight loss
		or alternatively, weight gain. Additional highly
-		ons are
		insulin resistance. Additional highly preferred
		indications are disorders of the musculoskeletal systems
		including myopathies, muscular dystrophy, and/or as
		described herein. Additional highly preferred
		indications include, hypertension, coronary artery disease,
		dyslipidemia, gallstones, osteoarthritis, degenerative
		arthritis, eating disorders, fibrosis, cachexia, and kidney
		diseases or disorders. Preferred indications include
		neoplasms and cancer, such as, lymphoma, leukemia and

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				breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
76 HCFLN88	290	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance.
			according to these assays are publicly	

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				Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are berein incomparated by reference in its	such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytonenia leukonenia thrombocytonenia acute
				are netern incorporated by reference in us entirety. T cells that may be used according to these assays are publicly	pancytopena, romopena, unonnocytopena, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis. AIDS, granulomatous disease.
				available (e.g., through the ATCC).	inflammatory bowel disease, sepsis, neutropenia,
				Exemplary mouse T cells that may be used according to these assays include the HT?	neutrophilia, psoriasis, suppression of immune reactions to transulanted organs and tissues. hemonhilia
				cell line, which is a suspension culture of	hypercoagulation, diabetes mellitus, endocarditis,
	٠			IL-2 dependent T cells that also respond to IL-4.	meningitis, Lyme Disease, and asthma and allergy.
76 HCI	HCFLN88	290	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
				(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth.	include autoimmune diseases (e.g., rheumatoid arthritis,
				Exemplary assays for transcription through	systemic lupus erythematosis, Crohn's disease, multiple
				the SRE that may be used or routinely	sclerosis and/or as described below), immunodeficiencies
				modified to test SRE activity of the	(e.g., as described below), boosting a T cell-mediated
				polypeptides of the invention (including	immune response, and suppressing a T cell-mediated
				antibodies and agonists or antagonists of	immune response. Additional highly preferred indications
				the invention) include assays disclosed in	include inflammation and inflammatory disorders, and
				Berger et al., Gene 66:1-10 (1998); Cullen	treating joint damage in patients with rheumatoid arthritis.
				and Malm, Methods in Enzymol 216:362-	An additional highly preferred indication is sepsis.
· · ·			,	308 (1992); Henthorn et al., Proc Nati	Highly preferred indications include neoplastic diseases
				Acad Sci USA \$5:6342-6346 (1988);	(e.g., leukemia, lymphoma, and/or as described below
				Benson et al., J Immunol 153(9):3862-	under "Hyperproliterative Disorders"). Additionally,
				3873 (1994); and Black et al., Virus Genes	highly preferred indications include neoplasms and
				12(2):105-117 (1997), the content of each	cancers, such as, for example, leukemia, lymphoma,
				of which are herein incorporated by	melanoma, glioma (e.g., malignant glioma), solid tumors,
				reference in its entirety. Mouse T cells	and prostate, breast, lung, colon, pancreatic, esophageal,
				that may be used according to these assays	stomach, brain, liver and urinary cancer. Other preferred
				are publicly available (e.g., through the	indications include benign dysproliferative disorders and

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				may be used according to these assays include the HT2 cell line, which is an IL-2 dependent suspension culture of T cells that also respond to IL-4.	hyperplastic conditions, such as, for example, hyperplastic conditions, such as, for example, hyperplastia, metaplastia, and/or dysplastia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
77	HCFLT90	591	Upregulation of CD152 and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such activation of cell surface markers, such activation of cell surface markers.	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity," "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,

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				Such assays that may be used or routinely modified to test immunomodulatory	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
78	HCHAB84	592	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
	_			example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
-				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar

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				can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or	coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux by polypeptides of the invention (including	endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in: Satin LS, et al., Endocrinology,	impaired wound nearing, and infection (e.g., infectious diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	skin), carpal tunnel syndrome and Dupuytren's
				3):847-51 (1992); and, Meats, JE, et al.,	obesit
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
	-			herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., inrougn the AICC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include HITTIS	
				Cells. HITT15 are an adherent epithelial	
				cell line established from Syrian hamster	
				islet cells transformed with SV40. These	
	-			cells express glucagon, somatostatin, and	
				glucocorticoid receptors. The cells secrete	
				insulin, which is stimulated by glucose and	
				glucagon and suppressed by somatostatin	
				or glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
79	HCMSX51	593	Regulation of apoptosis	Caspase Apoptosis. Assays for caspase	A highly preferred indication is diabetes mellitus.
			in pancreatic beta cells.	apoptosis are well known in the art and	An additional highly preferred indication is a complication
				may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,
				assess the autility of polypeptides of the	ulaucue liepliiopatiiy, kiuliey ulsease (e.g., leliai laliule,

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	invention (including antibodies and	nephropatny and/or other diseases and disorders as
	agonists or antagonists of the invention) to	described in the "Renal Disorders" section below), diabetic
	promote caspase protease-mediated	neuropathy, nerve disease and nerve damage (e.g., due to
	apoptosis. Apoptosis in pancreatic beta is	diabetic neuropathy), blood vessel blockage, heart disease,
	associated with induction and progression	stroke, impotence (e.g., due to diabetic neuropathy or
	of diabetes. Exemplary assays for	blood vessel blockage), seizures, mental confusion,
	caspase apoptosis that may be used or	drowsiness, nonketotic hyperglycemic-hyperosmolar
	routinely modified to test capase apoptosis	coma, cardiovascular disease (e.g., heart disease,
	activity of polypeptides of the invention	atherosclerosis, microvascular disease, hypertension,
	(including antibodies and agonists or	stroke, and other diseases and disorders as described in the
	antagonists of the invention) include the	"Cardiovascular Disorders" section below), dyslipidemia,
	assays disclosed in: Loweth, AC, et al.,	endocrine disorders (as described in the "Endocrine
	FEBS Lett, 400(3):285-8 (1997); Saini,	Disorders" section below), neuropathy, vision impairment
	KS, et al., Biochem Mol Biol Int,	(e.g., diabetic retinopathy and blindness), ulcers and
	39(6):1229-36 (1996); Krautheim, A., et	impaired wound healing, and infection (e.g., infectious
	al., Br J Pharmacol, 129(4):687-94 (2000);	diseases and disorders as described in the "Infectious
	Chandra J, et al., Diabetes, 50 Suppl	Diseases" section below, especially of the urinary tract and
	1:S44-7 (2001); Suk K, et al., J Immunol,	skin), carpal tunnel syndrome and Dupuytren's
-	166(7):4481-9 (2001); Tejedo J, et al.,	contracture). An additional highly preferred
	FEBS Lett, 459(2):238-43 (1999); Zhang,	indication is obesity and/or complications associated with
	S., et al., FEBS Lett, 455(3):315-20	obesity. Additional highly preferred indications include
	(1999); Lee et al., FEBS Lett 485(2-3):	weight loss or alternatively, weight gain. Aditional
	122-126 (2000); Nor et al., J Vasc Res	highly preferred indications are complications associated
	37(3): 209-218 (2000); and Karsan and	with insulin resistance.
	Harlan, J Atheroscler Thromb 3(2): 75-80	
	(1996); the contents of each of which are	
	herein incorporated by reference in its	
	entirety. Pancreatic cells that may be used	
	according to these assays are publicly	
	available (e.g., through the ATCC) and/or	
	may be routinely generated. Exemplary	
	pancreatic cells that may be used	
	according to these assays include RIN-m.	
	RIN-m is a rat adherent pancreatic beta	
	cell insulinoma cell line derived from a	
	radiation induced transplantable rat islet	
	cell tumor. The cells produce and secrete	

				islet polypeptide hormones, and produce insulin, somatostatin, and possibly olugation ATTC: #CRI -2057 Chick et	
				al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	
08	HCNC011	594	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renai failure,
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
			,	is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	tunnel
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preterred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
				(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	

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				pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	
81	HCNSD29	595	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious Diseases and disorders as described in the "Infectious Skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications include weight loss or alternatively, weight gain.

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			according to these assays are publicly	WILL HISUILL ICSISTATIOC.
			available (e.g., through the ATCC) and/or may be routinely generated. Exemplary	
			pancreatic cells that may be used	
			according to these assays include rat INS-1	
			line established from cells isolated from an	
			X-ray induced rat transplantable	
			insulinoma. These cells retain	
			characteristics typical of native pancreatic	
			beta cells including glucose inducible	
			insulin secretion. References: Asfari et al.	
			Endocrinology 1992 130:167.	
нсовн72	596	Regulation of viability	Assays for the regulation of viability and	A highly preferred indication is diabetes mellitus.
		and proliferation of	proliferation of cells in vitro are well-	An additional highly preferred indication is a complication
		pancreatic beta cells.	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
			polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
			antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
			the invention) to regulate viability and	neuropathy, nerve disease and nerve damage (e.g., due to
			proliferation of pancreatic beta cells. For	diabetic neuropathy), blood vessel blockage, heart disease,
			example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
•			cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
			viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
			quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
			signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
			active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
			used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
			regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
			pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
			invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
			agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
			include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
			BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
			(2001); Huotari MA, et al., Endocrinology,	skin), carpal tunnel syndrome and Dupuytren's

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Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An alternative highly preferred embodiment of the invention includes a method for decreasing adipocyte survival. A preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a
(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity
	Activation of Adipocyte P13 Kinase Signalling Pathway
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that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including	method for inhibiting adipocyte differentiation. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders").
antibodies and agonists or antagonists of the invention) include assays disclosed in	Preferred indications include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described below under
Forrer et al., Biol Chem 379(8-9):1101-	"Hyperproliferative Disorders"), blood disorders (e.g.,
1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schrever et al.,	hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, imporence and/or as
Diabetes 48(8):1662-1666 (1999), the	described below under "Immune Activity",
contents of each of which are herein	"Cardiovascular Disorders", and/or "Blood-Related
incorporated by reference in its entirety.	Disorders"), immune disorders (e.g., as described below
Mouse adipocyte cells that may be used	under "Immune Activity"), neural disorders (e.g., as
according to these assays are publicly	described below under "Neural Activity and Neurological
available (e.g., through the ATCC).	on (e.§
 Exemplary mouse adipocyte cells that may	<u>`</u>
be used according to these assays include	is diabetes mellitus. An additional highly preferred
3T3-L1 cells. 3T3-L1 is an adherent	indication is a complication associated with diabetes (e.g.,
mouse preadipocyte cell line that is a	diabetic retinopathy, diabetic nephropathy, kidney disease
continous substrain of 3T3 fibroblast cells	(e.g., renal failure, nephropathy and/or other diseases and
 developed through clonal isolation and	disorders as described in the "Renal Disorders" section
undergo a pre-adipocyte to adipose-like	below), diabetic neuropathy, nerve disease and nerve
conversion under appropriate	damage (e.g, due to diabetic neuropathy), blood vessel
differentiation conditions known in the art.	blockage, heart disease, stroke, impotence (e.g., due to
•	diabetic neuropathy or blood vessel blockage), seizures,
	mental confusion, drowsiness, nonketotic hyperglycemic-
	hyperosmolar coma, cardiovascular disease (e.g., heart
	disease, atherosclerosis, microvascular disease,
	hypertension, stroke, and other diseases and disorders as
	described in the "Cardiovascular Disorders" section
	below), dyslipidemia, endocrine disorders (as described in
	the "Endocrine Disorders" section below), neuropathy,
	vision impairment (e.g., diabetic retinopathy and
	blindness), ulcers and impaired wound healing, infection
	(e.g., infectious diseases and disorders as described in the
	"Infectious Diseases" section below, especially of the
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	Dupuyfren's contracture). An additional highly

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83	,	597	Regulation of	Assays for the regulation of transcription	preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma, liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is diabetes mellitus.
			transcription through the PEPCK promoter in hepatocytes	through the PEPCK promoter are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the PEPCK promoter in a reporter construct and regulate liver gluconeogenesis. Exemplary assays for regulation of transcription through the PEPCK promoter that may be used or routinely modified to test for PEPCK promoter activity (in hepatocytes) of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in	An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetes (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine

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	Berger et al., Gene 66:1-10 (1998); Cullen and Malm. Methods in Enzymol 216:362-	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and
	368 (1992); Henthorn et al., Proc Natl	impaired wound healing, infection (e.g., an infectious
	Acad Sci USA 85:6342-6346 (1988);	diseases or disorders as described in the "Infectious
	Lochhead et al., Diabetes 49(6):896-903	Diseases" section below, especially of the urinary tract and
	(2000); and Yeagley et al., J Biol Chem	skin), carpal tunnel syndrome and Dupuytren's
	275(23):17814-17820 (2000), the contents	contracture). An additional highly preferred indication
	of each of which is herein incorporated by	is obesity and/or complications associated with obesity.
	reference in its entirety. Hepatocyte cells	ndication
	that may be used according to these assays	or alternatively, weight gain. Additional highly
	are publicly available (e.g., through the	preferred indications are complications associated with
	ATCC) and/or may be routinely generated.	insulin resistance. Additional highly preferred
	Exemplary liver hepatoma cells that may	indications are disorders of the musculoskeletal systems
	be used according to these assays include	including myopathies, muscular dystrophy, and/or as
	H4lle cells, which contain a tyrosine amino	described herein. Additional highly preferred
	transferase that is inducible with	indications include glycogen storage disease (e.g.,
	glucocorticoids, insulin, or cAMP	glycogenoses), hepatitis, gallstones, cirrhosis of the liver,
	derivatives.	degenerative or necrotic liver disease, alcoholic liver
		diseases, fibrosis, liver regeneration, metabolic disease,
		dyslipidemia and cholesterol metabolism, and
		hepatocarcinomas. Highly preferred indications
•		include blood disorders (e.g., as described below under
		"Immune Activity", "Cardiovascular Disorders", and/or
		"Blood-Related Disorders"), immune disorders (e.g., as
		described below under "Immune Activity"), infection (e.g.,
		an infectious disease and/or disorder as described below
		under "Infectious Disease"), endocrine disorders (e.g., as
		described below under "Endocrine Disorders"), and neural
		elow under "N
		and Neurological Diseases"). Additional
		preferred indications include neoplastic diseases (e.g., as
		described below under "Hyperproliferative Disorders").
		Preferred indications include neoplasms and cancers, such
		as, leukemia, lymphoma, prostate, breast, lung, colon,
		pancreatic, esophageal, stomach, brain, and urinary cancer.
		A highly preferred indication is liver cancer. Other
		preferred indications include benion dysproliferative

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					disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
83	96ЭЭЭЭН	597	Activation of Skeletal	Kinase assay. Kinase assays, for examplek	Highly preferred indications include endocrine
			Muscie Cell EKK Signalling Pathway	EIK-1 Kinase assays, for EKK signal transduction that regulate cell proliferation	disorders (e.g., as described below under Endocrine Disorders") and disorders of the musculoskeletal system.
			f	or differentiation are well known in the art	Preferred indications include neoplastic diseases (e.g., as
				and may be used or routinely modified to	described below under "Hyperproliferative Disorders"),
				assess the ability of polypeptides of the	blood disorders (e.g., as described below under "Immune
				invention (including antibodies and	Activity", "Cardiovascular Disorders", and/or "Blood-
				agonists or antagonists of the invention) to	Related Disorders"), immune disorders (e.g., as described
				promote or inhibit cell proliferation,	below under "Immune Activity"), neural disorders (e.g., as
				activation, and differentiation. Exemplary	described below under "Neural Activity and Ineurological
				assays for ERK kinase activity that may be	on (e
				used or routinely modified to test EKK	·
				Kinase-induced activity of polypeptides of	is diabetes menitus. An additional inguisty preferred
				the invention (including antibodies and	indication is a complication associated with diabetes (e.g.,
				agonists or antagonists of the invention)	diabetic retinopathy, diabetic nephropathy, kidney disease
				include the assays disclosed in Forrer et	(e.g., renal failure, nephropathy and/or other diseases and
				al., Biol Chem 379(8-9):1101-1110	disorders as described in the "Renal Disorders" section
				(1998); Le Marchand-Brustel Y, Exp Clin	below), diabetic neuropathy, nerve disease and nerve
				Endocrinol Diabetes 107(2):126-132	damage (e.g., due to diabetic neuropathy), blood vessel
				(1999); Kyriakis JM, Biochem Soc Symp	blockage, heart disease, stroke, impotence (e.g., due to
				64:29-48 (1999); Chang and Karin, Nature	diabetic neuropathy or blood vessel blockage), seizures,
	-			410(6824):37-40 (2001); and Cobb MH,	mental confusion, drowsiness, nonketotic hyperglycemic-
				Prog Biophys Mol Biol 71(3-4):479-500	hyperosmolar coma, cardiovascular disease (e.g., heart
				(1999); the contents of each of which are	disease, atherosclerosis, microvascular disease,
				herein incorporated by reference in its	hypertension, stroke, and other diseases and disorders as
				entirety. Rat myoblast cells that may be	described in the "Cardiovascular Disorders" section
				used according to these assays are publicly	below), dyslipidemia, endocrine disorders (as described in
				available (e.g., through the ATCC).	the "Endocrine Disorders" section below), neuropathy,
				Exemplary rat myoblast cells that may be	vision impairment (e.g., diabetic retinopathy and
				used according to these assays include L6	blindness), ulcers and impaired wound healing, infection
				cells. L6 is an adherent rat myoblast cell	(e.g., infectious diseases and disorders as described in the
				line, isolated from primary cultures of rat	"Infectious Diseases" section below, especially of the
				thigh muscle, that fuses to form	rpal
				multinucleated myotubes and striated	Dupuytren's contracture). An additional highly
				HOERS AUET CUITUTE III UTITETEINIAUON MEURA.	preferred indication is openly and of complications

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) CUS6 598	invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, and differentiation. Exemplary activation, and differentiation. Exemplary activation, and differentiation. Exemplary preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110
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 Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
 (1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred

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				indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or
85 HCQCM24	599	Production of RANTES	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed	A highly preferred embodiment of the invention includes a method for stimulating RANTES production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) RANTES production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A most highly preferred indication includes AIDS and/or the prevention or reduction of HIV infection. Additional highly preferred indication includes immune disorders, for example, inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytic anemia (AI) plasmacytomas multiple

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86 HCRAY10 600	Production of IFNgamma using a T cells	in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407 (1995), the contents of each of which are herein incorporated by reference in its entirety. Human immune cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function and/or mediate	myeloma, Burkiti's lymphoma, arthritis, asthma, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms, such as, for example, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. An alternative highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infections granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response, and indications include inflammatory and indications include inflammatory and indications include inflammatory and indications include inflammatory and indications include inflam
		humoral or cell-mediated immunity. Exemplary assays that test for	idiopathic pulmonary fibrosis. Highly preferred indications include neoplastic diseases (e.g., leukemia,

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				od of other printed and the company	manhom malanama and/or as described below under
				initiation of outobines such as Interferon	"Hymerntaliferative Disorders". Highly preferred
				production of cytokines, such as microcon	Trypeipionicianic Disolucis). Triginiy prefered
				gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
				cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
				routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
				immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
				polypeptides of the invention (including	include benign dysproliferative disorders and pre-
				antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
				the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
				in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
				Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
				Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
				Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
				(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
				15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
				(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
				of each of which are herein incorporated	
				by reference in its entirety. Human T cells	
				that may be used according to these assays	
				may be isolated using techniques disclosed	
				herein or otherwise known in the art.	
				Human T cells are primary human	
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
87	HCRBF72	109	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,

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pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, authritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endergy.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune
the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and
	Production of IL-6
	602
	HCRNF78
	88

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chronic hymerneviliferative diseases	Activity" "Blood-Related Disorders" and/or
Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
or routinely modified to assess the ability	preferred indications also include boosting a B cell-
of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
the invention) to mediate	indications include inflammation and inflammatory
immunomodulation and differentiation and	disorders. Additional highly preferred indications include
modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
 include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
reference in its entirety. Human dendritic	ĭ
cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
disclosed herein or otherwise known in the	described below under "Infectious Disease").
 art. Human dendritic cells are antigen	
 presenting cells in suspension culture,	
which, when activated by antigen and/or	

				cytokines, initiate and upregulate T cell	
68	HCUAF85	603	Activation of transcription through NFKB response element in epithelial cells (such as HELA cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of epithhelial genes. Exemplary assays for transcription through the NFKB response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Kaltschmidt B, et al., Oncogene, 18(21):3213-3225 (1999); Beetz A, et al., Int J Radiat Biol, 76(11):1443-1453 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al., Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include include inflammation and inflammatory disorders.
06	HCUCF89	604	Protection from	HELA cell line. Caspase Apoptosis Rescue. Assays for	A highly preferred embodiment of the invention
\$	1100010	100	I IOCCUON HOM	Caspase Apopuosis incorne. Assays in	א וווצווו) עובינוכת בוונססתווובוור סו חוב ווועבוויסוו

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Endothelial Cell	caspase apoptosis rescue are well known in	caspase apoptosis rescue are well known in includes a method for stimulating endothelial cell growth.
Apoptosis.	the art and may be used of rounnely	An alternative nignty preferred emoodiment of the invention includes a mathod for inhibiting and otherial call
_	modified to assess the ability of the	miveling includes a meniod for diministrating endouncing con
	polypepudes of the invention (including	growin. A mignify preferred embodiment of the invastion includes a mathod for attimulating and atholical
	alitiodules aliti agoliists of alitagoliists of	miverition includes a include 101 stillinating chacking
	the invention) to infinite caspase protease-	cen promeranon. An anternative nigniy preferred
	mediated apoptosis. Exemplary assays for	embodiment of the invention includes a method for
	caspase apoptosis that may be used or	inhibiting endothelial cell proliferation. A highly
	routinely modified to test caspase	preferred embodiment of the invention includes a method
	apoptosis rescue of polypeptides of the	for stimulating endothelial cell growth. An alternative
	invention (including antibodies and	highly preferred embodiment of the invention includes a
	agonists or antagonists of the invention)	method for inhibiting endothelial cell growth. A
	include the assays disclosed in Romeo et	highly preferred embodiment of the invention includes a
,	al., Cardiovasc Res 45(3): 788-794 (2000);	method for stimulating apoptosis of endothelial cells. An
	Messmer et al., Br J Pharmacol 127(7):	alternative highly preferred embodiment of the invention
	1633-1640 (1999); and J Atheroscler	includes a method for inhibiting (e.g., decreasing)
	Thromb 3(2): 75-80 (1996); the contents of	apoptosis of endothelial cells. A highly preferred
	each of which are herein incorporated by	embodiment of the invention includes a method for
 	reference in its entirety. Endothelial cells	stimulating angiogenisis. An alternative highly preferred
	that may be used according to these assays	embodiment of the invention includes a method for
	are publicly available (e.g., through	inhibiting angiogenesis. A highly preferred
	commercial sources). Exemplary	embodiment of the invention includes a method for
	endothelial cells that may be used	reducing cardiac hypertrophy. An alternative highly
	according to these assays include bovine	preferred embodiment of the invention includes a method
	aortic endothelial cells (bAEC), which are	for inducing cardiac hypertrophy. Highly preferred
	an example of endothelial cells which line	indications include neoplastic diseases (e.g., as described
	blood vessels and are involved in functions	below under "Hyperproliferative Disorders"), and
	that include, but are not limited to,	disorders of the cardiovascular system (e.g., heart disease,
	angiogenesis, vascular permeability,	congestive heart failure, hypertension, aortic stenosis,
	vascular tone, and immune cell	cardiomyopathy, valvular regurgitation, left ventricular
	extravasation.	dysfunction, atherosclerosis and atherosclerotic vascular
		disease, diabetic nephropathy, intracardiac shunt, cardiac
		hypertrophy, myocardial infarction, chronic hemodynamic
		overload, and/or as described below under
		"Cardiovascular Disorders"). Highly preferred
		indications include cardiovascular, endothelial and/or
		angiogenic disorders (e.g., systemic disorders that affect

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vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications	that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred	indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal	disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma	(capillary and cavernous), glomus tumors, telangiectasia,	oachida y angionidaesis, irchidaigiochachedhai, angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, preast, rung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary		dysproliferative disorders and pre-neoplastic conditions,	example, hyperplasia, metaplasia, and/or	uyspiasia. — mgmy preferred murcanons asso metuda arterial disease, such as, atherosclerosis, hypertension,	ides,	'n,	aneurysms, restenosis; venous and lymphatic disorders	such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular	Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	(e.g., vascular injury such as, injury resulting from balloon	lant	fixation, scarring, ischemia reperfusion injury, rheumatoid	arinfitis, cereorovascular disease, renai diseases such as acute renal failure, and osteonorosis. Additional highly	tion,	diabetic or other retinopathies, thrombotic and coagulative	xual ad treatr
vessels such as diabetes mellitus, as well as diseases o vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indicative statements.	r cardiovasculari that inhibit angiog Highly preferred	indications include antiangiogenic activity to treat so tumors, leukemias, and Kaposi's sarcoma, and retinal	disorders. Highly preferred indications include neop and cancer, such as, Kaposi's sarcoma, hemangioma	ors, telai	oacinary angromatosis, inclinarignocinounicinoma, angriosarcoma, haemangropericytoma, lymphar	indicati	nicidue canceis such as, prostate, preast, fung, coron, pancreatic, esophageal, stomach, brain, liver, and uri	enign	olastic co	such as, for example, hyperplasia, metaplasia, and/or	s, hyper	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	phatic d	s, and ly rinheral	ed indic	and inju	sulting fi	angioplasty, and atheroschlerotic lesions), implant	ı ınjury,	i disease Addit	preferred indications include stroke, graft rejection,	otic and	disorders, vascularitis, lymph angiogenesis, sexual
is, as we the arter ally prefe	or card s that in Highl	nic activis sarcor	ications arcoma,	nus tumo	ytoma,	referred	tc, orcas h, brain	cancer. Preferred indications include benign	pre-neor	sia, meta	sclerosi	matory	d's phen	and lym	hangitis ch as ne	prefer	, burns,	njury res	ic lesion	erfusion	se, renai Prosis.	roke, gr	thromb	ingiogen devener
s mellitu h as of t s). High	tnat stimulate angiogenesis and/c Highly preferred are indications and/or cardiovascularization.	angioge Kaposi'	rred ind	is), glon	gioperic	lighly pr	stomac	ations in	ers and p	yperplas	athero	, inflam	Reynauc	venous	is, fymp rders sii	Highly	wounds	ıch as, ir	schlerot	mia rep	arinfilis, cerebrovascular disease, ren acute renal failure, and osteoporosis.	clude st	pathies,	lymph a
diabetes ves, suc nphatics	ngiogen d are in isculariz	ude anti ias, and	ly prefe h as, Ka	avernou	haeman,	oma. F	phageal,	ed indic	disord	ımple, h Iiahly, n	such as	disease	ase and	enosis;	ophlebii Ilar diso	ncer.	such as	njury su	d athero	ig, ische	ovascui ure, and	ations ir	er retino	ularitis, related r
such as themsel	nulate a preferre cardiova	ons incl	rs. High Icer, suc	ry and c	y angio ircoma,	ngiosar	tic, eso	Preferr	iferative	, for exa	disease	y artery	d's dise	sms, resi	thromb	disease, and cancer.	trauma	ascular i	asty, an	ı, scarrii	s, cereor	ed indic	c or othe	rs, vasc
vessels vessels veins an	that stir Highly and/or	indicati tumors,	disorde and car	(capilla	angiosa	lympha	pancrea	cancer.	dysprol	such as	dyspiasia. arterial dise	corona	Reynan	aneurys	such as	disease	include	(e.g., v	angiopl	fixation	arthritis	preferr	diabetion	disorde
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 HCUCK44	605	Protection from Endothelial Cell Apoptosis.	et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line. Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to inhibit caspase proteasemediated apoptosis. Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis rescue of polypeptides of the invention) include the assays disclosed in Romeo et al., Cardiovasc Res 45(3): 788-794 (2000);	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An method for stimulating aboptosis of endothelial cells.
			Messmer et al., Br J Pharmacol 127(7): 1633-1640 (1999); and J Atheroscler	alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing)
			Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by	apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for
			reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through	stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred

and continued to the follow under "Hyperpoliferative Disorders"), and continued to below under "Hyperpoliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, vascular permeability, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels stemselves, such as of the arteries, capillaries, veins and/or cardiovascularization. Highly preferred are indications shall simulate angiogenesis and/or cardiovascularization. Highly preferred and cancer, such as Maposi's sarcoma, and retinal disorders. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancers such as, Faposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and uninary cancer. Preferred indications include benign
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coronary artery disease, inflammatory vasculitides, Reynaud's disease and Reynaud's phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional
	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of
	Production of MCP-1
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	HCUCK44
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				polypeptides of the invention (including	highly preferred indications include inflammation and
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
				contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
			-	according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or
				using techniques disclosed herein or	dysplasia.
				otherwise known in the art. Human	
				dendritic cells are antigen presenting cells	
				in suspension culture, which, when	
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
				and functional activities.	
92	HCUDD64	909	Production of GM-CSF	GM-CSF FMAT. GM-CSF is expressed	A highly preferred embodiment of the invention
·				by activated T cells, macrophages,	includes a method for stimulating the production of GM-
				endothelial cells, and fibroblasts. GM-	CSF. An alternative highly preferred embodiment of the

	OCD and differentiation and	المرفودية
	proliferation of granulocytes- macrophage	of GM-CSF. Highly preferred indications include
	progenitors and enhances antimicrobial	a
	activity in neutrophils, monocytes and	
	macrophage. Additionally, GM-CSF plays	below under "Infectious Disease". Highly preferred
	an important role in the differentiation of	indications include blood disorders (e.g., neutropenia (and
	dendritic cells and monocytes, and	the prevention of neutropenia (e.g., in HIV infected
•	increases antigen presentation. GM-CSF	patients), and/or as described below under "Immune
	is considered to be a proinflammatory	Activity", "Blood-Related Disorders", and/or
	cytokine. Assays for immunomodulatory	"Cardiovascular Disorders"). Highly preferred indications
	proteins that promote the production of	also include autoimmune diseases (e.g., rheumatoid
	GM-CSF are well known in the art and	arthritis, systemic lupus erythematosis, multiple sclerosis
	may be used or routinely modified to	and/or as described below) and immunodeficiencies (e.g.,
	assess the ability of polypeptides of the	as described below). Additional highly preferred
	invention (including antibodies and	indications include asthma. Highly preferred indications
	agonists or antagonists of the invention) to	include neoplastic diseases (e.g., leukemia (e.g., acute
	mediate immunomodulation and modulate	lymphoblastic leukemia, and acute myelogenous
	the growth and differentiation of	leukemia), lymphoma (e.g., non-Hodgkin's lymphoma and
	leukocytes. Exemplary assays that test for	Hodgkin's disease), and/or as described below under
	immunomodulatory proteins evaluate the	"Hyperproliferative Disorders"). Highly preferred
	production of cytokines, such as GM-CSF,	indications include neoplasms and cancers, such as,
	and the activation of T cells. Such assays	leukemia, lymphoma, melanoma, and prostate, breast,
	that may be used or routinely modified to	lung, colon, pancreatic, esophageal, stomach, brain, liver
	test immunomodulatory activity of	and urinary cancer. Other preferred indications include
	polypeptides of the invention (including	benign dysproliferative disorders and pre-neoplastic
	antibodies and agonists or antagonists of	conditions, such as, for example, hyperplasia, metaplasia,
	the invention) include the assays disclosed	and/or dysplasia. Highly preferred indications include:
	in Miraglia et al., J Biomolecular	suppression of immune reactions to transplanted organs
	Screening 4:193-204 (1999); Rowland et	and tissues (e.g., bone marrow transplant); accelerating
	al., "Lymphocytes: a practical approach"	myeloid recovery; and mobilizing hematopoietic
	Chapter 6:138-160 (2000); and Ye et al., J	progenitor cells. Preferred indications include boosting
	Leukoc Biol (58(2):225-233, the contents	a T cell-mediated immune response, and alternatively,
	of each of which are herein incorporated	suppressing a T cell-mediated immune response.
	by reference in its entirety. Natural killer	Preferred indications include anemia, pancytopenia,
	cells that may be used according to these	leukopenia, thrombocytopenia, acute lymphocytic anemia
	assays are publicly available (e.g., through	(ALL), plasmacytomas, multiple myeloma, Burkitt's
	the ATCC) or may be isolated using	lymphoma, arthritis, AIDS, granulomatous disease,

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				known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.	inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy.
55	HCUDD64	909	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al., Biochem Mol Biol Int, 39(6):1229-36 (1996); Krautheim, A., et al., Br J Pharmacol, 129(4):687-94 (2000); Chandra J, et al., Diabetes, 50 Suppl 1:S44-7 (2001); Suk K, et al., I Immunol, 166(7):4481-9 (2001); Tejedo J, et al., FEBS Lett, 455(2):315-20 (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlon I Arthory I Athendral I I	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease, (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with highly preferred indications are complications associated with highly preferred indications are complications associated

				(1996); the contents of each of which are herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980	
63	HCWAE64	607	Regulation of transcription via DMEF1 response element in adipocytes and pre-adipocytes	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious

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diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.		A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications
test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Thai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human	Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under annomiate	differentiation culture conditions. Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
		Activation of transcription through serum response element in immune cells (such as T-cells).
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				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to bind the	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factor and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
_				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary human T cells, such	indications include anemia, pancytopenia, leukopenia,
				as the MOLT4, that may be used according	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				to these assays are publicly available (e.g.,	anemia (ALL), plasmacytomas, multiple myeloma,
				through the ATCC).	Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Intectious Disease").
93	HCWAE64	209	Activation of transcription through	Assays for the activation of transcription through the Signal Transducers and	A highly preferred indication is allergy. Another highly preferred indication is asthma.

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			STAT6 response	Activators of Transcription (STAT6)	highly preferred indications include inflammation and
			element in immune	response element are well-known in the art	inflammatory disorders. Preferred indications
			cells (such as natural	and may be used or routinely modified to	include blood disorders (e.g., as described below under
			killer cells).	assess the ability of polypeptides of the	"Immune Activity", "Blood-Related Disorders", and/or
				invention (including antibodies and	"Cardiovascular Disorders"). Preferred indications include
				agonists or antagonists of the invention) to	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				regulate STAT6 transcription factors and	lupus erythematosis, multiple sclerosis and/or as described
				modulate the expression of multiple genes.	below) and immunodeficiencies (e.g., as described below).
				Exemplary assays for transcription through	Preferred indications include neoplastic diseases (e.g.,
				the STAT6 response element that may be	leukemia, lymphoma, melanoma, and/or as described
				used or routinely modified to test STAT6	below under "Hyperproliferative Disorders"). Preferred
				response element activity of the	indications include neoplasms, such as, for example,
				polypeptides of the invention (including	leukemia, lymphoma, melanoma, and prostate, breast,
				antibodies and agonists or antagonists of	lung, colon, pancreatic, esophageal, stomach, brain, liver
				the invention) include assays disclosed in	and urinary cancer. Other preferred indications include
				Berger et al., Gene 66:1-10 (1998); Cullen	benign dysproliferative disorders and pre-neoplastic
				and Malm, Methods in Enzymol 216:362-	conditions, such as, for example, hyperplasia, metaplasia,
				368 (1992); Henthorn et al., Proc Natl	and/or dysplasia. Preferred indications include
				Acad Sci USA 85:6342-6346 (1988);	anemia, pancytopenia, leukopenia, thrombocytopenia,
				Georas et al., Blood 92(12):4529-4538	Hodgkin's disease, acute lymphocytic anemia (ALL),
				(1998); Moffatt et al., Transplantation	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				69(7):1521-1523 (2000); Curiel et al., Eur	arthritis, AIDS, granulomatous disease, inflammatory
				J Immunol 27(8):1982-1987 (1997); and	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				Masuda et al., J Biol Chem	suppression of immune reactions to transplanted organs
				275(38):29331-29337 (2000), the contents	and tissues, hemophilia, hypercoagulation, diabetes
				of each of which are herein incorporated	mellitus, endocarditis, meningitis, and Lyme Disease.
				by reference in its entirety. T cells that	Additional preferred indications include infection (e.g., an
				may be used according to these assays are	infectious disease as described below under "Infectious
				publicly available (e.g., through the	Disease").
				ATCC). Exemplary rat natural killer cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC).	
6	HCWAE64	209	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			In infinure cells (such	Known in the art and may be used or	indications include neoplasms and cancers, such as, for

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			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma.
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
		•		Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
			-	4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
				as the SUPT cell line, that may be used	include anemia, pancytopenia, leukopenia,
				according to these assays are publicly	thrombocytopenia, acute lymphocytic anemia (ALL),
				available (e.g., through the ATCC).	plasmacytomas, multiple myeloma, arthritis, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, neutropenia, neutrophilia, psoriasis, suppression of
					immune reactions to transplanted organs and tissues,
					hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
į					allergy.
93	HCWAE64	209	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			INFAI TESPONSE	cells (INFA1) response element are well-	Biood-Keialed Disorders, and/or Cardiovascular
			element in immune	known in the art and may be used or	Disorders"). Highly preferred indications include
			cens (such as natural	routinely incurring to assess the admity of	autominimic diseases (e.g., incumatori atmitts, systemic

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lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AlDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
killer cells).	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
		-		Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
				used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
94	HCWFU39	809	Upregulation of CD71 and activation of T cells	CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An
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carrying protein that is expressed	includes a method for inhibiting T cell proliferation
prometation: CD/11 is expressed predominantly on cells that are actively	Preferred indications include blood disorders (e.g., as
proliferating. Assays for	described below under "Immune Activity", "Blood-
immunomodulatory proteins expressed on	Related Disorders", and/or "Cardiovascular Disorders"),
activated T cells, B cells, and most	and infection (e.g., as described below under "Infectious
proliferating cells are well known in the art	Disease"). Highly preferred indications include
and may be used or routinely modified to	autoimmune diseases (e.g., rheumatoid arthritis, systemic
assess the ability of polypeptides of the	lupus erythematosis, multiple sclerosis and/or as described
invention (including antibodies and	below), immunodeficiencies (e.g., as described below),
agonists or antagonists of the invention) to	boosting a T cell-mediated immune response, and
modulate the activation of T cells, and/or	suppressing a T cell-mediated immune response.
mediate humoral or cell-mediated	Additional highly preferred indications include
immunity. Exemplary assays that test for	inflammation and inflammatory disorders. Additional
immunomodulatory proteins evaluate the	highly preferred indications include infection. Preferred
upregulation of cell surface markers, such	indications include neoplastic diseases (e.g., leukemia,
as CD71, and the activation of T cells.	lymphoma, and/or as described below under
Such assays that may be used or routinely	"Hyperproliferative Disorders"). Preferred indications
modified to test immunomodulatory	include neoplasms and cancers, such as, for example,
activity of polypeptides of the invention	leukemia, lymphoma, melanoma, and prostate, breast,
(including antibodies and agonists or	lung, colon, pancreatic, esophageal, stomach, brain, liver
antagonists of the invention) include, for	and urinary cancer. Other preferred indications include
example, the assays disclosed in Miraglia	benign dysproliferative disorders and pre-neoplastic
et al., J Biomolecular Screening 4:193-204	conditions, such as, for example, hyperplasia, metaplasia,
(1999); Rowland et al., "Lymphocytes: a	and/or dysplasia. Preferred indications include anemia,
practical approach" Chapter 6:138-160	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
(2000); and Afetra et al., Ann Rheum Dis	disease, acute lymphocytic anemia (ALL), plasmacytomas,
52(6):457-460 (1993), the contents of each	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
reference in its entirety. Human T cells	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
that may be used according to these assays	immune reactions to transplanted organs and tissues,
may be isolated using techniques disclosed	hemophilia, hypercoagulation, diabetes mellitus,
herein or otherwise known in the art.	endocarditis, meningitis, Lyme Disease, and asthma and
Human T cells are primary human	allergy.
lymphocytes that mature in the thymus and	
express a T Cell receptor and CD3, CD4,	
or CD8. These cells mediate humoral or	

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				cell-mediated immunity and may be preactivated to enhance responsiveness to	
				immunomodulatory factors.	
95	HCWUL09	609	Activation of	Assays for the activation of transcription	A highly preferred indication includes allergy. A
			transcription through	through the GATA3 response element are	highly preferred indication includes asthma. A highly
			GATA-3 response	well-known in the art and may be used or	preferred indication includes rhinitis. Additional highly
ŧ			element in immune	routinely modified to assess the ability of	preferred indications include infection (e.g., an infectious
			cells (such as T-cells).	polypeptides of the invention (including	disease as described below under "Infectious Disease"),
				antibodies and agonists or antagonists of	and inflammation and inflammatory disorders.
			•	the invention) to regulate GATA3	Preferred indications include blood disorders (e.g., as
				transcription factors and modulate	described below under "Immune Activity", "Blood-
				expression of genes important for Th2	Related Disorders", and/or "Cardiovascular Disorders").
				immune response development.	Preferred indications include autoimmune diseases (e.g.,
				Exemplary assays for transcription through	rheumatoid arthritis, systemic lupus erythematosis,
				the GATA3 response element that may be	multiple sclerosis and/or as described below) and
				used or routinely modified to test GATA3-	immunodeficiencies (e.g., as described below).
				response element activity of polypeptides	Preferred indications include neoplastic diseases (e.g.,
				of the invention (including antibodies and	leukemia, lymphoma, melanoma, and/or as described
				agonists or antagonists of the invention)	below under "Hyperproliferative Disorders"). Preferred
			-	include assays disclosed in Berger et al.,	indications include neoplasms and cancer, such as, for
				Gene 66:1-10 (1998); Cullen and Malm,	example, leukemia, lymphoma, melanoma, and prostate,
				Methods in Enzymol 216:362-368 (1992);	breast, lung, colon, pancreatic, esophageal, stomach,
				Henthorn et al., Proc Natl Acad Sci USA	brain, liver and urinary cancer. Other preferred indications
				85:6342-6346 (1988); Flavell et al., Cold	include benign dysproliferative disorders and pre-
				Spring Harb Symp Quant Biol 64:563-571	neoplastic conditions, such as, for example, hyperplasia,
				(1999); Rodriguez-Palmero et al., Eur J	metaplasia, and/or dysplasia. Preferred indications
				Immunol 29(12):3914-3924 (1999); Zheng	include anemia, pancytopenia, leukopenia,
				and Flavell, Cell 89(4):587-596 (1997);	thrombocytopenia, leukemias, Hodgkin's disease, acute
				and Henderson et al., Mol Cell Biol	lymphocytic anemia (ALL), plasmacytomas, multiple
				14(6):4286-4294 (1994), the contents of	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				each of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
				reference in its entirety. T cells that may	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				be used according to these assays are	immune reactions to transplanted organs and tissues,
•				publicly available (e.g., through the	hemophilia, hypercoagulation, diabetes mellitus,
				ATCC). Exemplary mouse T cells that	endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays	
				include the H12 cell line, which is a	

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				suspension culture of IL-2 dependent T cells that also respond to IL-4.	
96	HDHAA42	610	Production of	IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using	role in the immune system and is	includes a method for stimulating the production of IFNg.
			Ivatulai Milici Celis	cytokine. IFNg promotes TH1 and	An alternative inginy preferred embodiment of the invention includes a method for inhibiting the production
				inhibits TH2; promotes IgG2a and inhibits	of IFNg. Highly preferred indications include blood
				IgE; induces macrophage activation; and	disorders (e.g., as described below under "Immune
				increases MHC expression. Assays for	Activity", "Blood-Related Disorders", "Hyperproliferative
	•.			immunomodulatory proteins produced by	Disorders" (e.g. cancer/tumorigenesis) and/or
				T cells and NK cells that regulate a variety	"Cardiovascular Disorders"), and infection (e.g., viral
				of inflammatory activities and inhibit TH2	infections, tuberculosis, infections associated with chronic
				helper cell functions are well known in the	granulomatosus disease and malignant osteoporosis,
				art and may be used or routinely modified	and/or as described below under "Intectious Disease").
				to assess the ability of polypeptides of the	Highly preferred indications include autoimmune disease
				invention (including antibodies and	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				agonists or antagonists of the invention) to	multiple sclerosis and/or as described below),
				mediate immunomodulation, regulate	immunodeficiency (e.g., as described below), boosting a T
				inflammatory activities, modulate TH2	cell-mediated immune response, and suppressing a T cell-
				helper cell function, and/or mediate	mediated immune response, boosting antibody-dependent
				humoral or cell-mediated immunity.	immune responses, suppressing antibody-dependent
				Exemplary assays that test for	immune responses, boosting innate immunity and immune
				immunomodulatory proteins evaluate the	responses, and suppressing innate immunity and immune
				production of cytokines, such as Interferon	responses. Additional highly preferred indications include
				gamma (IFNg), and the activation of T	inflammation and inflammatory disorders. Additional
				cells. Such assays that may be used or	preferred indications include idiopathic pulmonary
				routinely modified to test	fibrosis. Highly preferred indications include neoplastic
				immunomodulatory activity of	diseases (e.g., leukemia, lymphoma, melanoma, and/or as
				polypeptides of the invention (including	described below under "Hyperproliferative Disorders").
				antibodies and agonists or antagonists of	Highly preferred indications include neoplasms and
				the invention) include the assays disclosed	cancers, such as, for example, leukemia, lymphoma,
				in Miraglia et al., J Biomolecular	melanoma, and prostate, breast, lung, colon, pancreatic,
				Screening 4:193-204 (1999); Rowland et	esophageal, stomach, brain, liver and urinary cancer.
				al., "Lymphocytes: a practical approach"	Other preferred indications include benign dysproliferative
				Chapter 6:138-160 (2000); Gonzalez et al.,	disorders and pre-neoplastic conditions, such as, for
				J Clin Lab Anal 8(5):225-233 (1995);	example, hyperplasia, metaplasia, and/or dysplasia.
				Dilliau et al., Ailli IV I Acau Sei 630.22-32	riefereu muranons incidue anemia, pancytopema,

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				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
			-	(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
		-		reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
86	HDPCW16	612	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention
			MIP1alpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An
				activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
				monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
				chemotaxis are well known in the art and	production. A highly preferred indication is infection
				may be used or routinely modified to	Š
				assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
				invention (including antibodies and	blood disorders (e.g., as described below under "Immune
		,		agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
				mediate immunomodulation, modulate	Cardiovascular Disorders). Hignly preferred indications

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	differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et	
	for immunomodulatory proteins evalue for immunomodulatory proteins evalue production of chemokines, such macrophage inflammatory protein 1 (MIP-1a), and the activation of monocytes/macrophages and T cells assays that may be used or routinely modified to test immunomodulatory chemotaxis activity of polypeptides invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lympha a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drake	_
	the production of chemokines, such macrophage inflammatory protein 1 (MIP-1a), and the activation of monocytes/macrophages and T cells assays that may be used or routinely modified to test immunomodulatory chemotaxis activity of polypeptides invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lympha a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Draks	
	macrophage inflammatory protein I (MIP-1a), and the activation of monocytes/macrophages and T cells assays that may be used or routinely modified to test immunomodulatory chemotaxis activity of polypeptides invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Draks	
	macropnage inflammatory protein I (MIP-1a), and the activation of monocytes/macrophages and T cells assays that may be used or routinely modified to test immunomodulatory chemotaxis activity of polypeptides invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Draks	
	(MIP-1a), and the activation of monocytes/macrophages and T cells assays that may be used or routinely modified to test immunomodulatory chemotaxis activity of polypeptides invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Draks	
	monocytes/macrophages and T cells assays that may be used or routinely modified to test immunomodulatory chemotaxis activity of polypeptides invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Draks	_
	assays that may be used or routinely modified to test immunomodulatory chemotaxis activity of polypeptides invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Draks	
	modified to test immunomodulatory chemotaxis activity of polypeptides invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drak	
	chemotaxis activity of polypeptides invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drak	
	invention (including antibodies and agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drak	
	agonists or antagonists of the invent include assays disclosed in Miraglia J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drak	
	include assays disclosed in Miraglia J Biomolecular Screening 4:193- 204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drak	
	J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drak	
	204(1999); Rowland et al., "Lymph a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drak	
	a practical approach" Chapter 6:138 (2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drak	
	(2000); Satthaporn and Eremin, J R Surg Ednb 45(1):9-19 (2001); Drak	
	Surg Ednb 45(1):9-19 (2001); Drak	
		_
	al., Transp Immunol 8(1):17-29 (2000);); as, leukemia, lymphoma, prostate, breast, lung, colon,
	Verhasselt et al., J Immunol 158:2919-	
	2925 (1997); and Nardelli et al., J Leukoc	koc cancer. Other preferred indications include benign
	Biol 65:822-828 (1999), the contents of	if dysproliferative disorders and pre-neoplastic conditions,
_	each of which are herein incorporated by	by such as, for example, hyperplasia, metaplasia, and/or
	reference in its entirety. Human dendritic	
	cells that may be used according to these	Se
	assays may be isolated using techniques	S
	disclosed herein or otherwise known in the	the
	art. Human dendritic cells are antigen	
	presenting cells in suspension culture,	
	which, when activated by antigen and/or)r
	cytokines, initiate and upregulate T cell	
	proliferation and functional activities.	
98 HDPCW16 612 Production of IC	of ICAM-1 Assays for measuring expression of	Preferred embodiments of the invention include using
	ICAM-1 are well-known in the art and	polypeptides of the invention (or antibodies, agonists, or
	may be used or routinely modified to	antagonists thereof) in detection, diagnosis, prevention,
	assess the ability of polypeptides of the	and/or treatment of Inflammation, Vascular Disease,
	invention (including antibodies and	Athereosclerosis, Restenosis, and Stroke

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to n tal, of cly or e	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indication is sepsis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and
agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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				Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
100	HDPDJ58	614	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described

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Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
 (1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred

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				activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia	leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benien dysproliferative disorders and pre-neoplastic
		,		et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia,
				practical approach" Chapter 6:138-160 (2000); and Afetra et al., Ann Rheum Dis	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas,
				52(6):457-460 (1993), the contents of each	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				of which are nerein incorporated by reference in its entirety. Human T cells	granulomatous disease, initammatory bower disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of
	-			that may be used according to these assays	immune reactions to transplanted organs and tissues,
				may be isolated using techniques disclosed	hemophilia, hypercoagulation, diabetes mellitus,
				herein or otherwise known in the art.	endocarditis, meningitis, Lyme Disease, and asthma and
				Human T cells are primary human	allergy.
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
		•		or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
101 HDPFF10	开10	615	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention
			MIP1alpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An
				activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
				monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
				chemotaxis are well known in the art and	production. A highly preferred indication is infection
				may be used or routinely modified to	(e.g., an infectious disease as described below under
				assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
				invention (including antibodies and	blood disorders (e.g., as described below under "Immune
				agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
				mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
				chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
				differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
				for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
				the production of chemokines, such as	described below). Additional highly preferred indications
				macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
				(1911 - 1a), and the activation of	ricicited indications also include ancima, pancytopenia,

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monocytes/marcophages and 1 cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miragila et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1)9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardellie et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are breni incoporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. IL-6 FMAT. IL-6 is produced by T cells and innectional activities. IL-6 FMAT. IL-6 is produced by T cells and innectional activities. IL-6 FMAT. IL-6 is produced by T cells and innections in IR-4 induced IgB production and increases Is A production (IgA plays a role in mucosal immunity). IL-6 induces a role in mucosal immunity). IL-6 induces a role in mucosal immunity. IL-6 induces a role in mucosal immunity. IL-6 in production of IL-6 has been inked to audinimune of IL-6 has been inked to audinimune and increases a role in mucosal immunity.	monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., 1 Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J. R. Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., 1 Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirery. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell profluction and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in mucosal immunity). IL-6 induces cytokoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease a learned and an elementary.	monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., Tymphocytes: a practical approach "Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen andor cytokines, initiate and upregulate T cell proliferation and functional activities. Broduction of IL-6 participates in L-4 induced lgE production and increases lgA production (lgA plays a role in mucosal immunity). IL-6 induces cytokoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune dicases a leason of lacebase and lass strong effects on B cells. Inchasses of lacebase and
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			a large variety of cells where the	preferred indications include autoimmine diseases (e o
			evarescion level is strongly remilated by	rhenmatoid arthritis systemic lunus erythematosis
			capicssion icycl is suchigity regulated by	incumatona arumins, systemo rapas erymermatosis,
			cytokines, growth factors, and hormones	multiple scierosis and/or as described below) and
			are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
			or routinely modified to assess the ability	preferred indications also include boosting a B cell-
			of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
			antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
			the invention) to mediate	indications include inflammation and inflammatory
			immunomodulation and differentiation and	disorders. Additional highly preferred indications include
			modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
			Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
			immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
			production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
			the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
			proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
			Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
			modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
			diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
			the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
			agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
			include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
			J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
			a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
			(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
			158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
			each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
			reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
			cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
			assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
			disclosed herein or otherwise known in the	described below under "Infectious Disease").
		•	art. Human dendritic cells are antigen	
			presenting cells in suspension culture,	
			which, when activated by antigen and/or	
			cytokines, initiate and upregulate T cell	
\dashv			proliferation and functional activities.	
102 HDPFU43 616	9]	Activation of Skeletal	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention

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exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
well known in the art and may be used or	as described below under "Immune Activity", "Blood-
routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
 assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
 proteins evaluate the production of	Additional highly preferred indications include
cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
alpha (TNFa), and the induction or	. <u>:</u>
inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
routinely modified to test	leukemia, lymphoma, and/or as described below under
immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
 Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
 al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
be used according to these assays may be	ij
 isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
III suspenision cuiture, winch, when	Discase).

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103 HDPFY18	617	Activation of transcription through NFKB response element in immune cells (such as T-cells).	activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below), and immunodeficiencies (e.g., as indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperpoliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, disease, inflammatory bowel disease, acute lymphocytic neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.
HDPFY18	617	Upregulation of CD152 and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a

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Other preferred indications include benign dysproliferative "Cardiovascular Disorders"), Highly preferred indications method for inhibiting the activation of and/or inactivating systemic lupus erythematosis, multiple sclerosis and/or as below), boosting a T cell-mediated immune response, and proliferation. An alternative highly preferred embodiment blood disorders (e.g., as described below under "Immune described below), immunodeficiencies (e.g., as described reactions to transplanted organs and tissues, hemophilia, leukopenia, thrombocytopenia, Hodgkin's disease, acute of the invention includes a method for stimulating T cell include autoimmune diseases (e.g., rheumatoid arthritis, Highly preferred indications include neoplastic diseases melanoma, and prostate, breast, lung, colon, pancreatic, An Highly preferred indications include (e.g., leukemia, lymphoma, and/or as described below lymphocytic anemia (ALL), plasmacytomas, multiple esophageal, stomach, brain, liver and urinary cancer. under "Hyperproliferative Disorders"). Additionally, disorders and pre-neoplastic conditions, such as, for Preferred indications include anemia, pancytopenia, granulomatous disease, inflammatory bowel disease, cancers, such as, for example, leukemia, lymphoma, sepsis, neutropenia, neutrophilia, psoriasis, immune example, hyperplasia, metaplasia, and/or dysplasia. highly preferred indications include neoplasms and additional preferred indication is infection (e.g., as A highly preferred embodiment of the hypercoagulation, diabetes mellitus, endocarditis, invention includes a method for inhibiting T cell suppressing a T cell-mediated immune response. inflammatory disorders, and asthma and allergy. myeloma, Burkitt's lymphoma, arthritis, AIDS, described below under "Infectious Disease"). Activity", "Blood-Related Disorders", and/or meningitis, Lyme Disease, inflammation and proliferation. CD8+ T cells are well known in the art and expressed almost exclusively on CD4+ and agonists or antagonists of the invention) to 77(1):1-10 (1999); Oostervegal et al., Curr et al., J Biomolecular Screening 4:193-204 proliferation. Reduced CD152 expression the maintenance of T cell homeostasis and upregulation of cell surface markers, such Opin Immunol 11(3):294-300 (1999); and are herein incorporated by reference in its autoimmune diseases. Overexpression of immunomodulatory proteins important in immunity. Exemplary assays that test for Such assays that may be used or routinely example, the assays disclosed in Miraglia 321 (1998), the contents of each of which entirety. Human T cells that may be used according to these assays may be isolated has been linked to hyperproliferative and immunomodulatory proteins evaluate the (1999); Rowland et al., "Lymphocytes: a (2000); McCoy et al., Immunol Cell Biol antagonists of the invention) include, for activity of polypeptides of the invention Saito T, Curr Opin Immunol 10(3):313as CD152, and the activation of T cells. practical approach" Chapter 6:138-160 assess the ability of polypeptides of the may be used or routinely modified to including antibodies and agonists or modified to test immunomodulatory invention (including antibodies and maintain T cell homeostasis, and/or modulate the activation of T cells, mediate humoral or cell-mediated immunoresponses. Assays for CD152 may lead to impaired

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				using techniques disclosed herein or otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
104	HDPGE24	618	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
				(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
				Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
				Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
				865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
				Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
				Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
				Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
				of each of which is herein incorporated by	with insulin resistance.

e assays the nerated. y be ude terent Syrian SV40. ceptors. n and 7 7 Acad.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious
reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesis and its expression is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors. Exemplary assays that may be used or routinely modified to test for regulation of transcription of Malic Enzyme (in hepatocytes) by polypeptides of the
	Regulation of transcription of Malic Enzyme in hepatocytes
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diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating hepatocyte cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting hepatocyte cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating hepatocyte cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting hepatocyte cell differentiation. A highly preferred embodiment of the invention includes a method for activating hepatocyte cells. An alternative
invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Streeper, R.S., et al., Mol Endocrinol, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol Endocrinol, 8(10):1361-9 (1994); Barroso, I., et al., J Biol Chem, 274(25):17997-8004 (1999); Ijpenberg, A., et al., J Biol Chem, 272(32):20108-20117 (1997); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays includes the mouse 373-L1 cell line. 3T3-L1 is a mouse preadipocyte cell line (adherent). It is a continuous substrain of 3T3 fibroblasts developed through clonal isolation. Cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be
	Activation of Hepatocyte ERK Signaling Pathway
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highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating hepatocyte cells. Highly preferred indications include disorders of the liver and/or endocrine disorders (e.g., as described below under "Endocrine Disorders"). Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological	Diseases"), and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other	diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or
used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its	entirety. Rat liver hepatoma cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat liver hepatoma cells that may be used according to these assays include H4lle cells, which are known to respond to glucocorticoids, insulin, or cAMP derivatives.	

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complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hepatitis, jaundice, gallstones, cirrhosis of the liver, degenerative or necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and chlolesterol metabolism. Additional highly preferred indications and colon and pancreatic cancer. Preferred indications also include prostate, breast, lung, esophageal, stomach, brain, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dvsplasia.	
	Kinase assays, for example an Elk-1 kinase assay for ERK signal transduction that regulates cell proliferation or differentiation, are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Ali H, et al., J Immunol, 165(12):7215-7223 (2000);
	Regulation of proliferation and/or differentiation in immune cells (such as mast cells).
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	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders. Additional preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hubhy preferred indications include neoplastic diseases (e.g., leukemia, 'Hymphoma, melanoma, and/or as described below under "Hymphoma, melanoma, and/or as described below under "Hymphoma, preferred indications include neoplastic diseases (e.g., leukemia, 'Hymphoma, melanoma, and/or as described below under "Hymphoma, melanoma, and/or as described below under "Hymphoma preferred indications include neoplastic diseases (e.g., leukemia, 'Hymphoma, melanoma, and/or as described below under "Hymphoma, melanoma, and/or as described below under "Hymphoma, melanoma, and/or as described below under "Hymphoma preferred indications include neoplastic diseases (e.g., leukemia, 'Hymphoma, melanoma, and/or as described below under "Hymphoma preferred indications include neoplastic diseases (e.g., leukemia, 'Hymphoma preferred indications includ
Tam SY, et al., Blood, 90(5):1807-1820 (1997); Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Berra et al., Biochem Pharmacol 60(8):1171-1178 (2000); Gupta et al., Exp Cell Res 247(2):495-504 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells that may be used according to these assays include human mast cells such as the HMC-1 cell line.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by in T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 art helper cell functions are well known in the Hart and may be used or routinely modified (e to assess the ability of polypeptides of the minvention (including antibodies and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and mediate immunomodulation, regulate inhammatory activities, modulate TH2 helper cell function, and/or mediate inhumoral or cell-mediated immunity. Exemplary assays that test for inhimmunomodulatory proteins evaluate the lyproduction of cytokines, such as Interferon 'Y-
	Production of IENgamma using a T cells
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indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy) or
gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4,	or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from
	Insulin Secretion
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pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
assays that may be used or routinely	stroke, and other diseases and disorders as described in the
 modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
 (2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
Screening, 4.193-204 (1999), the contents	highly preferred indications are complications associated
 of each of which is herein incorporated by	with insulin resistance.
reference in its entirety. Pancreatic cells	
that may be used according to these assays	
are publicly available (e.g., through the	
ATCC) and/or may be routinely generated.	
Exemplary pancreatic cells that may be	
 used according to these assays include	
HITT15 Cells. HITT15 are an adherent	
 epithelial cell line established from Syrian	
hamster islet cells transformed with SV40.	
These cells express glucagon,	
somatostatin, and glucocorticoid receptors.	
The cells secrete insulin, which is	
stimulated by glucose and glucagon and	
suppressed by somatostatin or	
glucocorticoids. ATTC# CRL-1777	
Refs: Lord and Ashcroft. Biochem. J. 219:	
547-551; Santerre et al. Proc. Natl. Acad.	
Sci. USA 78: 4339-4343, 1981.	

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				RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	
107	HDPOL37	621	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indication inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is clude neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and indications include benign dysproliferative disorders and

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				publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below indas "Tribation").
108	HDPO076	622	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors,

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assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL—hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectious Disease.").	Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-polypeptides of the invention (including antibodies and agonists or antagonists or metabolism and cell survival. Exemplary assays for PI3 kinase activity of est PI3 kinase-induced activity of entibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in PCD:263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the cransduction that regulate glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity of antibodies and agonists or antagonists of the invention) include assays disclosed in Preferred indications include assays disclosed in Polypertension, congestive heart failure, blood vessel 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the cransduction that regulate glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity of antibodies and agonists or antagonists of the invention includes a method for inhibiting adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for simulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly prefe
assays are the ATCC may be us include th 2 depend with cytor	se Signalling
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incorporated by reference in its entirety. Mouse adjocyte cells that may be used a conding to these assays are publicity and reserved below under "Neural Activity and Neurological available (e.g., through the ATC). Exemplary mouse adjocyte cells that may be used described below under "Neural Activity and Neurological available (e.g., through the ATC). Exemplary mouse adjocyte cells that may be used according to these assays include "Infectious Disease"). A highly preferred indication is a complication associated with diabetes (e.g., mouse preadipocyte cell line that is a continous substrain of 313 fbroblast cells (e.g., renal failure, nephropathy and/or other diseases and developed through found isolation and below, diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve conversion under appropriate below, diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease, stocks, impotence (e.g., due to diabetic neuropathy, or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperension, stroke, and other disease (e.g., heart disease, theroselectoris, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders, section below, distorders as described in the "Endocrine Disorders, section below, vision impairment (e.g., diabetic returopathy and blindness), ulcers and impaired wound healing, infection associated with disease, daviditional highly preferred indications are disorders or on preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications include weight loss or alternatively, weight demisional public and disease dividitional highly preferred indications are disorders. Add	> i
incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.

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	gallstones, osteoarthritis, degenerative arinitis, eaung disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma, liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia,	ranscription through the API response element are API response element transcription through the API response element are API response element are API response element are In immune cells (such polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the API response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm., Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-3081 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety.
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transcription through the ATCC). Exemplary mouse T reactions to transplanted organs and tissues, endocarditis, and Lyme Disease. Activation of transcription through the API response element in immune cells (such polypeptides of the invention) to modulate growth and other cell functions. Exemplary assays for the activation for managonists of the invention in the invention in the centre of functions. Exemplary assays for the activation of transcription through the API response element and may be used or notatinely modified to assess the ability of the invention) to modulate growth and other cell functions. Exemplary assays for expense element and may be used or rotutinely modified to test API -response element activity of polypeptides of the invention) include assays disclosed in Berger et al., Gene (66:1-10 (1988); Cullen and Malin, Briot Chen 2524(9):2089(-2014 (1997); Appendix of the invention include and architis, systemic lupture and including antibodises and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene (66:1-10 (1988); Cullen and Malin, Briot Chen 2524(9):2089(-2014 (1989); Rystopic luptus of the invention) include assays disclosed in Berger et al., Gene (1997); Appendix and or as described below under assays disclosed in Berger et al., Gene (1997); Appendix and or as described below) and antiple soft and an argonists of the invention) include assays disclosed in Berger et al., Gene (1997); Appendix and or as described below under assays disclosed in Berger et al., Gene (1997); Appendix and or as described below) and antiple activity of polypeptides of the invention) include assays disclosed in Berger et al., Gene (1997); Appendix and or as described below under assays disclosed in Berger et al., Gene (1997); Appendix and or as described below under assays disclosed in a described below under assays disclosed and appendix and or as described below under assays disclosed and appendix and or as described below under assays disclosed and appendix and or assays disc
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				culture cell line.	
100	HDPPD03	869	Activation of	Assays for the activation of transcription	A highly preferred embodiment of the invention
61		<u> </u>	transcription through	through the CD28 response element are	includes a method for stimulating T cell proliferation. An
			CD28 resnonse element	well-known in the art and may be used or	alternative highly preferred embodiment of the invention
			in immine cells (such	routinely modified to assess the ability of	includes a method for inhibiting T cell proliferation. A
			as T-cells)	polypeptides of the invention (including	highly preferred embodiment of the invention includes a
				antibodies and agonists or antagonists of	method for activating T cells. An alternative highly
				the invention) to stimulate IL-2 expression	preferred embodiment of the invention includes a method
				in T cells. Exemplary assays for	for inhibiting the activation of and/or inactivating T cells.
				transcription through the CD28 response	A highly preferred embodiment of the invention includes a
				element that may be used or routinely	method for stimulating (e.g., increasing) IL-2 production.
				modified to test CD28-response element	An alternative highly preferred embodiment of the
				activity of polypeptides of the invention	S
				(including antibodies and agonists or	IL-2 production. Additional highly preferred
				antagonists of the invention) include	indications include inflammation and inflammatory
				assays disclosed in Berger et al., Gene	disorders. Highly preferred indications include
				66:1-10 (1998); Cullen and Malm,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
				Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
				85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
				Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. Highly
				(1997); Parra et al., J Immunol	preferred indications include neoplastic diseases (e.g.,
				166(4):2437-2443 (2001); and Butscher et	melanoma, renal cell carcinoma, leukemia, lymphoma,
				al., J Biol Chem 3(1):552-560 (1998), the	and/or as described below under "Hyperproliferative
				contents of each of which are herein	Disorders"). Highly preferred indications include
				incorporated by reference in its entirety. T	neoplasms and cancers, such as, for example, melanoma
				cells that may be used according to these	(e.g., metastatic melanoma), renal cell carcinoma (e.g.,
				assays are publicly available (e.g., through	metastatic renal cell carcinoma), leukemia, lymphoma
				the ATCC). Exemplary human T cells that	(e.g., T cell lymphoma), and prostate, breast, lung, colon,
				may be used according to these assays	pancreatic, esophageal, stomach, brain, liver and urinary
				include the SUPT cell line, which is a	cancer. Other preferred indications include benign
				suspension culture of IL-2 and IL-4	dysproliferative disorders and pre-neoplastic conditions,
				responsive T cells.	such as, for example, hyperplasia, metaplasia, and/or
					dysplasia. A highly preferred indication includes
					infection (e.g., AIDS, tuberculosis, infections associated
					with granulomatous disease, and osteoporosis, and/or as
					described below under misculous Discase 7: 11 mgmj

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preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include blood disorders ctivated T are well- Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include ability of autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperprolasia and/or as described benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperprolasia and/or as allore.
	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:632-6346 (1988); Serfling et al.
	Activation of transcription through NFAT response element in immune cells (such as T-cells).
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				2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
601	HDPPD93	623	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred

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			each of which are herein incorporated by	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			reference in its entirety. T cells that may	anemia (ALL), plasmacytomas, multiple myeloma,
			be used according to these assays are	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia,
			ATCC). Exemplary human T cells that	neutrophilia, psoriasis, hemophilia, hypercoagulation,
			may be used according to these assays	diabetes mellitus, endocarditis, meningitis, Lyme Disease,
			include the SUPT cell line, which is a	suppression of immune reactions to transplanted organs,
			suspension culture of IL-2 and IL-4	asthma and allergy.
+			responsive T cells.	
109 HDPPD93	623	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
		transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
		NFAT response	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
		element in immune	known in the art and may be used or	Disorders"). Highly preferred indications include
		cells (such as natural	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
		killer cells).	polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
			antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),
			the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
			transcription factors and modulate	suppressing a T cell-mediated immune response.
			expression of genes involved in	Additional highly preferred indications include
			immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
			assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
			response element that may be used or	disease as described below under "Infectious Disease").
			routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,
			element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
			invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
			agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
			include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
			Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
			Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
			Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
			85:6342-6346 (1988); Aramburu et al., J	such as, for example, hyperplasia, metaplasia, and/or
			Exp Med 182(3):801-810 (1995); De Boer	dysplasia. Preferred indications also include anemia,
			et al., Int J Biochem Cell Biol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
			31(10):1221-1236 (1999); Fraser et al., Eur	disease, acute lymphocytic anemia (ALL), plasmacytomas,
	_		J Immunol 29(3):838-844 (1999); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
			Yeseen et al., J Biol Chem 268(19):14285-	granulomatous disease, inflammatory bowel disease,
			14293 (1993), the contents of each of	sepsis, neutropenia, neutrophilia, psoriasis, suppression of

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				which are herein incorporated by reference	immune reactions to transplanted organs and tissues,
				in its entirety. NK cells that may be used	hemophilia, hypercoagulation, diabetes mellitus,
				according to these assays are publicly	endocarditis, meningitis, Lyme Disease, astinma and
				Exemplary human NK cells that may be	and By.
				used according to these assays include the	
				NK-YT cell line, which is a human natural	
				killer cell line with cytolytic and cytotoxic	
\dashv				activity.	
110 HDPI	НЪРРQ30	624	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
			•	is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
	-			pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
,				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
·				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
				(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.

E	HDPPW82	625	Upregulation of CD71 and activation of T cells	according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167. CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells, B cells, and most proliferating cells are well known in the art	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include
	,			and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD71, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional highly preferred indications include infection. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include

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				chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al.,	granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus,
				J Biomolecular Screening 4:193- 204(1999); Rowland et al., "Lymphocytes:	endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g. lenkemia lymphoma and/or as described
				(2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et	below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers. such
				al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-	as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary
				2925 (1997); and Nardelli et al., J Leukoc Biol 65:822 828 (1990), the contents of	cancer. Other preferred indications include benign
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
112	HDPXN20	979		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	incl
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
				helper cell functions are well known in the	Highly preferred indications include autoimmune disease
				art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),

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Ill Volleto or contracting animodates and	cell-mediated immine response and suppressing a T cell-
agomets of amagomets of the invention) to	confined and intitude assessment of difficult highly professed
mediate immunomodulation, regulate	mediated immune response. Additional ingnity preferred
inflammatory activities, modulate 1 H2	indications include inflammation and inflammatory
helper cell function, and/or mediate	disorders. Additional preferred indications include
humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
polypeptides of the invention (including	include benign dysproliferative disorders and pre-
antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
 of each of which are herein incorporated	
by reference in its entirety. Human T cells	
that may be used according to these assays	
may be isolated using techniques disclosed	
herein or otherwise known in the art.	
Human T cells are primary human	
 lymphocytes that mature in the thymus and	
express a T Cell receptor and CD3, CD4,	
or CD8. These cells mediate humoral or	
cell-mediated immunity and may be	
preactivated to enhance responsiveness to	
immunomodulatory factors.	
immunomodulatory factors.	

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	nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar	atherosclerosis, microvascular disease, hypertensi stroke, and other diseases and disorders as descril "Cardiovascular Disorders" section below), dyslip endocrine disorders (as described in the "Endocri Disorders" section below), neuropathy, vision im (e.g., diabetic retinopathy and blindness), ulcers a impaired wound healing, and infection (e.g., infediseases and disorders as described in the "Infecti Diseases" section below, especially of the urinary skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associa	weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain	key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and,	Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40.
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			These cells express glucagon, somatostatin, and glucocorticoid receptors.	
			The cells secrete insulin, which is	
			stimulated by glucose and glucagon and	
			suppressed by somatostatin or	
			glucocorticoids. ATTC# CRL-1777	
			Refs: Lord and Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc. Natl. Acad.	
			Sci. USA 78: 4339-4343, 1981.	
114 HDTAU35	628	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
			and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
			participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
			and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
			role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
			cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
			of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
			disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
			chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
			Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
			differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
			a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
			expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
			cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
			are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
			or routinely modified to assess the ability	preferred indications also include boosting a B cell-
			of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
			antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
			the invention) to mediate	indications include inflammation and inflammatory
			immunomodulation and differentiation and	disorders. Additional highly preferred indications include
			modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
			Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
			immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
	•		production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
			the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
			proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
			Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
			modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.

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				differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities	Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
114	HDTAU35	628	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple

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114 HDTAU35 628 Production of TNF alpha by dendritic cells	modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Sathhaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/on as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include alood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease multiple clause remultiple endocations include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease
	immunomodulation, modulate inflammation and cytotoxicity. Exemplary	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and

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			assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and unregulate T cell proliferation	suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., Hyperproliferative Disorders'). Additionally, highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectious disease as described below under "Infectious Disease").
115 HDTAV54	629	Production of TNF alpha by dendritic cells	and functional activities. TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and contoxic effects on a variety of cells are	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g.,

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	To be sure but the out at the live of	as described below under "Immine Activity". "Blood-
- 1-	Well Allowed in the district of the oblight of	Delated Disorders", and/or "Cardiovascular Disorders").
	10dillici) illodillica to assess die activity of	Highly preferred indications include autoimmine diseases
	polypepudes of the invention (including	(e g rhenmatoid arthritis systemic lunus erythematosis.
	the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
	imminomodulation, modulate	below), immunodeficiencies (e.g., as described below),
	inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
	assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
	proteins evaluate the production of	Additional highly preferred indications include
	cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
	alpha (TNFa), and the induction or	
	inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
-	response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
-	routinely modified to test	leukemia, lymphoma, and/or as described below under
	immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
	polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
	antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
	the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
	Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
	4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
	"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
	Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
	al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
	(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
	160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
	al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
	Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
	(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
	herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
	entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
	be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
	isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
	or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
	dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
	in suspension culture, which, when	Disease").
	activated by antigen and/or cytokines,	
	initiate and unregulate T cell proliferation	

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				and functional activities.	
116	HDTFX18	630	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	æ
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	s a
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
-				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	
_				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
				that may be used according to these assays	additional highly preferred indication is a complication
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
				adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
				is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
				cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
				and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
				TIKE CUITVEISIUII UITUCI APPIUDITATE	diadetic ticutopatity), blood vessel blockage, ticat disease,

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				differentiation conditions known in the art	stroke impotence (e.g. due to diabetic neuronathy or
					blood vessel blockage), seizures, mental confusion,
					drowsiness, nonketotic hyperglycemic-hyperosmolar
					coma, cardiovascular disease (e.g., heart disease,
					atherosclerosis, microvascular disease, hypertension,
					stroke, and other diseases and disorders as described in the
					"Cardiovascular Disorders" section below), dyslipidemia,
-					endocrine disorders (as described in the "Endocrine
					Disorders" section below), neuropathy, vision impairment
					(e.g., diabetic retinopathy and blindness), ulcers and
					impaired wound healing, infection (e.g., infectious
					diseases and disorders as described in the "Infectious
					Diseases" section below (particularly of the urinary tract
					and skin). An additional highly preferred indication is
					obesity and/or complications associated with obesity.
					Additional highly preferred indications include weight loss
					or alternatively, weight gain. Additional highly
					preferred indications are complications associated with
					insulin resistance. Additional highly preferred
					indications are disorders of the musculoskeletal systems
					including myopathies, muscular dystrophy, and/or as
-				-	described herein. Additional highly preferred
					indications include, hypertension, coronary artery disease,
					dyslipidemia, gallstones, osteoarthritis, degenerative
					arthritis, eating disorders, fibrosis, cachexia, and kidney
					diseases or disorders. Preferred indications include
					neoplasms and cancer, such as, lymphoma, leukemia and
					breast, colon, and kidney cancer. Additional preferred
					indications include melanoma, prostate, lung, pancreatic,
					esophageal, stomach, brain, liver, and urinary cancer.
					Highly preferred indications include lipomas and
					liposarcomas. Other preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
					dysplasia.
117	HDTGW48	631	Activation of transcription through	Assays for the activation of transcription through the NFKB response element are	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or

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antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Autoimmunity, Allergy and Asthma	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection
well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438 (1998); Pyatt DW, et al., Cell Biol Toxicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the Reh according to these assays include the Reh	MIP-Ialpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and
NFKB response element in immune cells (such as B-cells).	Production of MIP1alpha
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Illay be used of fourified in	(e.g., an infectious disease as described below under
 assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
invention (including antibodies and	blood disorders (e.g., as described below under "Immune
agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
the production of chemokines, such as	described below). Additional highly preferred indications
macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
(MIP-1a), and the activation of	Preferred indications also include anemia, pancytopenia,
monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
 invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
 J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
 2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
reference in its entirety. Human dendritic	dysplasia.
cells that may be used according to these	
assays may be isolated using techniques	
disclosed herein or otherwise known in the	
art. Human dendritic cells are antigen	
presenting cells in suspension culture,	
 which, when activated by antigen and/or	
cytokines, initiate and upregulate T cell	
proliferation and functional activities.	

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nvention includes ? 3) TNF alpha d embodiment of th nulating (e.g., Preferred indicat cribed below under I Disorders", and/or y preferred indicat rheumatoid arthritis 1's disease, multiple a T cell-mediated I T cell-mediated Iy preferred indicat I cell-mediated Iy preferred indicat	the rheumatoid arthradion is sepsis. In explastic disease is described below is?). Additionally, neoplasms and mia, lymphoma, glioma), solid tume	ncreatic, esophage: uncer. Other preferr erative disorders a or example, blasia. Preferred penia, leukopenia, se, acute lymphocy tiple myeloma, i, granulomatous i, granulomatous i, neutropenia, of immune reactior nophilia, endocarditis, eperfusion injury, i
A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications	treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors,	and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and
Prode prode investigated in the prode in the production in the prode i	High (e.g. unde high canc mela	stom indiciple i
Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and	agonasis of anagonasis of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T	cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.
Activation of transcription through serum response element in immune cells (such as T-cells).		
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					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
119	HE2CA60	633	Production of IL-4	IL-4 FMAT. Assays for immunomodulatory proteins secreted by	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4
				1 HZ cells that sumulate B cells, 1 cells, macrophages and mast cells and promote	production. An alternative inglify preferred embodinien of the invention includes a method for inhibiting (e.g.,
				polarization of CD4+ cells into TH2 cells	reducing) IL-4 production. A highly preferred
				are well known in the art and may be used	indication includes asthma. A highly preferred
				of fourmery modified to assess the ability of polypeptides of the invention (including	indication includes after gy. A figury preferred indication includes rhinitis. Additional highly preferred
				antibodies and agonists or antagonists of	indications include inflammation and inflammatory
				the invention) to mediate	disorders. Highly preferred indications include
				immunomodulation, stimulate immune	neoplastic diseases (e.g., leukemia, lymphoma,
				cells, modulate immune cell polarization,	melanoma, and/or as described below under
		-		and/or mediate humoral or cell-mediated	"Hyperproliferative Disorders"). Preferred indications
				immunity. Exemplary assays that test for	include neoplasms and cancers, such as, for example,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and prostate, breast,
				production of cytokines, such as IL-4, and	lung, colon, pancreatic, esophageal, stomach, brain, liver
				the stimulation of immune cells, such as B	and urinary cancer. Other preferred indications include
				cells, T cells, macrophages and mast cells.	benign dysproliferative disorders and pre-neoplastic
				Such assays that may be used or routinely	ıs, fo
				modified to test immunomodulatory	and/or dysplasia. Preferred indications include blood
		-		activity of polypeptides of the invention	disorders (e.g., as described below under "Immune
•				(including antibodies and agonists or	Activity", "Blood-Related Disorders", and/or
				antagonists of the invention) include the	"Cardiovascular Disorders"). Preferred indications include
				assays disclosed in Miraglia et al., J	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				Biomolecular Screening 4:193-204 (1999);	lupus erythematosis, multiple sclerosis and/or as described
				Rowland et al., "Lymphocytes: a practical	below) and immunodeficiencies (e.g., as described below).
				approach" Chapter 6:138-160 (2000);	Preferred indications include anemia, pancytopenia,
				Gonzalez et al., J Clin Lab Anal 8(5):277-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				283 (1194); Yssel et al., Res Immunol	lymphocytic anemia (ALL), plasmacytomas, multiple
				144(8):610-616 (1993); Bagley et al., Nat	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				Immunol 1(3):257-261 (2000); and van der	granulomatous disease, inflammatory bowel disease,
			-	Graaff et al., Rheumatology (Oxford)	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				38(3):214-220 (1999), the contents of each	immune reactions to transplanted organs and tissues,
				of which are nerein incorporated by	nemopnilia, nypercoagulation, diabetes mellitus,

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				reference in its entirety. Human T cells	endocarditis, meningitis, and Lyme Disease. An
				may be isolated using techniques disclosed	infectious disease as described below under "Infectious
				herein or otherwise known in the art.	Disease").
				Human T cells are primary human	
_				lymphocytes that mature in the thymus and	
				express a T cell receptor and CD3, CD4, or	
				CD8. These cells mediate humoral or cell-	
				mediated immunity and may be	
			-	preactivated to enhance responsiveness to	
				immunomodulatory factors.	
120	HE2CA60	634	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
. —			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
		-		the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
			-	Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
		-		Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse I cells that	indications include benign dysproliterative disorders and

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				may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease")
120	HE2CA60	634	Production of IL-4	IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immune cells, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-4 production. A highly preferred indication includes asthma. A highly preferred indication includes rhinitis. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include Activity", "Blood-Related Disorders", and/or

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autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include include inflammation and inflammatory disorders.
assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human Ilymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention
	Activation of transcription through GAS response element in epithelial cells (such as HELA cells).
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diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention
	A highly preferred embincludes a method for increalternative highly preferred
test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Thai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice.", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under appropriate	differentiation culture conditions. Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose
	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway
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	 brown in the art and may be seed or	A mestared ambodiment of the invention includes a
	continuity modified to access the ability of	mothed for etimulating manage cell meditemation.
	Toutined infomined to assess the ability of	inculod for stiffiniating muscle cell profiteration. In a
	polypeptides of the invention (including	specific embodiment, skeletal muscle cell proliferation is
	antibodies and agonists or antagonists of	stimulated. An alternative highly preferred embodiment of
	the invention) to promote or inhibit	the invention includes a method for inhibiting muscle cell
	glucose metabolism and cell survival.	proliferation. In a specific embodiment, skeletal muscle
	Exemplary assays for PI3 kinase activity	cell proliferation is inhibited. A preferred embodiment
	that may be used or routinely modified to	of the invention includes a method for stimulating muscle
	test PI3 kinase-induced activity of	cell differentiation. In a specific embodiment, skeletal
	polypeptides of the invention (including	muscle cell differentiation is stimulated. An alternative
	antibodies and agonists or antagonists of	highly preferred embodiment of the invention includes a
	the invention) include assays disclosed in	method for inhibiting muscle cell differentiation. In a
	Forrer et al., Biol Chem 379(8-9):1101-	specific embodiment, skeletal muscle cell differentiation is
	1110 (1998); Nikoulina et al., Diabetes	inhibited. Highly preferred indications include disorders
	49(2):263-271 (2000); and Schreyer et al.,	of the musculoskeletal system. Preferred indications
	Diabetes 48(8):1662-1666 (1999), the	include neoplastic diseases (e.g., as described below under
	contents of each of which are herein	"Hyperproliferative Disorders"), endocrine disorders (e.g.,
	incorporated by reference in its entirety.	as described below under "Endocrine Disorders"), neural
	Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
	according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
	available (e.g., through the ATCC).	described below under "Immune Activity",
	Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
	used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
	cells. L6 is an adherent rat myoblast cell	under "Immune Activity"), and infection (e.g., as
	line, isolated from primary cultures of rat	described below under "Infectious Disease"). A
	thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus.
	multinucleated myotubes and striated	additional highly preferred indication is a complication
	fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
		diabetic nephropathy, kidney disease (e.g., renal failure,
		nephropathy and/or other diseases and disorders as
		described in the "Renal Disorders" section below), diabetic
		neuropathy, nerve disease and nerve damage (e.g, due to
-		diabetic neuropathy), blood vessel blockage, heart disease,
-		stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,

					atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infections (e.g., infectious
					Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal system including myonathies.
					described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions,
124	HE2P093	638	Activation of Adipocyte PI3 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 assays, for P13 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An alternative highly preferred embodiment of the invention includes a method for decreasing adipocyte survival. A preferred embodiment of the invention for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a

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	antibodies and agonists or antagonists of	
	the invention) to promote or inhibit	preferred embodiment of the invention includes a method
	glucose metabolism and cell survival.	for stimulating adipocyte differentiation. An alternative
	Exemplary assays for PI3 kinase activity	highly preferred embodiment of the invention includes a
	that may be used or routinely modified to	method for inhibiting adipocyte differentiation. Highly
	test PI3 kinase-induced activity of	preferred indications include endocrine disorders (e.g., as
	polypeptides of the invention (including	described below under "Endocrine Disorders").
	antibodies and agonists or antagonists of	Preferred indications include neoplastic diseases (e.g.,
	the invention) include assays disclosed in	lipomas, liposarcomas, and/or as described below under
	Forrer et al., Biol Chem 379(8-9):1101-	"Hyperproliferative Disorders"), blood disorders (e.g.,
	1110 (1998); Nikoulina et al., Diabetes	hypertension, congestive heart failure, blood vessel
	49(2):263-271 (2000); and Schreyer et al.,	blockage, heart disease, stroke, impotence and/or as
	Diabetes 48(8):1662-1666 (1999), the	described below under "Immune Activity",
	contents of each of which are herein	"Cardiovascular Disorders", and/or "Blood-Related
	incorporated by reference in its entirety.	Disorders"), immune disorders (e.g., as described below
	Mouse adipocyte cells that may be used	under "Immune Activity"), neural disorders (e.g., as
	according to these assays are publicly	described below under "Neural Activity and Neurological
	available (e.g., through the ATCC).	Diseases"), and infection (e.g., as described below under
	Exemplary mouse adipocyte cells that may	"Infectious Disease"). A highly preferred indication
	be used according to these assays include	is diabetes mellitus. An additional highly preferred
	3T3-L1 cells. 3T3-L1 is an adherent	indication is a complication associated with diabetes (e.g.,
	mouse preadipocyte cell line that is a	diabetic retinopathy, diabetic nephropathy, kidney disease
	continous substrain of 3T3 fibroblast cells	(e.g., renal failure, nephropathy and/or other diseases and
	developed through clonal isolation and	disorders as described in the "Renal Disorders" section
	undergo a pre-adipocyte to adipose-like	below), diabetic neuropathy, nerve disease and nerve
	conversion under appropriate	damage (e.g, due to diabetic neuropathy), blood vessel
	differentiation conditions known in the art.	blockage, heart disease, stroke, impotence (e.g., due to
		diabetic neuropathy or blood vessel blockage), seizures,
		mental confusion, drowsiness, nonketotic hyperglycemic-
		hyperosmolar coma, cardiovascular disease (e.g., heart
,		disease, atherosclerosis, microvascular disease,
		hypertension, stroke, and other diseases and disorders as
		described in the "Cardiovascular Disorders" section
		below), dyslipidemia, endocrine disorders (as described in
		the "Endocrine Disorders" section below), neuropathy,
		vision impairment (e.g., diabetic retinopathy and
		blindness), ulcers and impaired wound healing, infection

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				(e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma, liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and prenenaplasia, and/or dysplasia.
124 HE2P093	638	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated

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				wide variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
				assays for transcription through the cAMP	response. Additional preferred indications include
				response element that may be used or	inflammation and inflammatory disorders. Highly
				routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
				agonists or antagonists of the invention)	indications include neoplasms and cancers, such as, for
				include assays disclosed in Berger et al.,	example, leukemia, lymphoma (e.g., T cell lymphoma,
				Gene 66:1-10 (1998); Cullen and Malm,	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				Methods in Enzymol 216:362-368 (1992);	disease), melanoma, and prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver and urinary
				85:6342-6346 (1988); Black et al., Virus	cancer. Other preferred indications include benign
				Genes 15(2):105-117 (1997); and	dysproliferative disorders and pre-neoplastic conditions,
				Belkowski et al., J Immunol 161(2):659-	such as, for example, hyperplasia, metaplasia, and/or
				665 (1998), the contents of each of which	dysplasia. Preferred indications include anemia,
				are herein incorporated by reference in its	pancytopenia, leukopenia, thrombocytopenia, acute
				entirety. T cells that may be used	lymphocytic anemia (ALL), plasmacytomas, multiple
				according to these assays are publicly	myeloma, arthritis, AIDS, granulomatous disease,
				available (e.g., through the ATCC).	inflammatory bowel disease, sepsis, neutropenia,
				Exemplary mouse T cells that may be used	neutrophilia, psoriasis, suppression of immune reactions to
				according to these assays include the	transplanted organs and tissues, hemophilia,
				CTLL cell line, which is a suspension	hypercoagulation, diabetes mellitus, endocarditis,
				culture of IL-2 dependent cytotoxic T	meningitis, Lyme Disease, and asthma and allergy.
				cells.	
125 HI	HE6AU52	639	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
			- 1 - 1	expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,

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				cytokines, growth factors, and hormones are well known in the art and may be used	multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
125	HE6AU52	639	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred

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	smooth muscle, and other cell types that	embodiment of the invention includes a method for
	exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
	cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
	well known in the art and may be used or	as described below under "Immune Activity", "Blood-
	routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
	polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
	antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
	the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
	immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
	inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
	assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
	proteins evaluate the production of	Additional highly preferred indications include
	cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
	alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
	inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
	response. Such assays that may be used or	Š
	routinely modified to test	leukemia, lymphoma, and/or as described below under
	immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
	polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
	antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
	the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
	Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
	4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
	"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
	Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
	al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
	(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
	160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
	al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
	Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
	(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
	herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
	entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
	be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
	isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
	or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
	dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious

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				in suspension culture, which, when	Disease").
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation and functional activities.	
126	HE6CS65	640	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
	,			participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
	-			differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute

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lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes
204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., I Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include
	Production of MCP-1
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assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Biomolecular Screening 4:193-204(1990); Biomolecular and viral All Mary 1:193-204(1990); Biomolecular All Mary 1:193-204(1990); Biomo	immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory activity activated below. A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection assess the ability of polypeptides of the invention assess the ability of polypeptides of the includes a method for simulating MIP1a production. A highly preferred indication is infection. A highly preferred indication is infection assess the ability of polypeptides of the invention includes a method for simhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection assess the ability of polypeptides of the invention and inflammate of the invention. An influed in include and assays that test include autoimmune disease as described below under "Immune agonists of the invention include autoimmune diseases (e.g., as described below under "Immune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Additional highly preferred indications include anemia, pancytopenia, include inflammatory disorders. (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and monocytes/macrophage inflammatory disorders. [Amphocytic anemia (AlLL), plasmacytomas, multiple activation of hemotytes/macrophage and T cells. Such assays that may be used or routinely modified to test immunomodulatory and includes a method for inhibition of test immunomodulatory and i
	Production of MIP lalpha
	149
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	127

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chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., 1 Biomolecular Screening 4:193- a practical approach" (Chapter 6:138-160 (2000); Sathaporn and Eremin, 1 R Coll (2000); Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., 1 Immunol 158:2919- cancer. Other preferred indications include neoplastic each of which are herein incorporated by such at. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cells are antigen presenting agonists or antagonists of the invention and functional activities.	ough ement such
	Activation of transcription through GAS response elemen in immune cells (such as T-cells).
	642
	HE6EY13
	128

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129	HE6FU11	643	Regulation of apoptosis in pancreatic beta cells.	activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Hentinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC). Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis and activity of polypeptides of the invention (including antibodies and agonists or	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders (e.g., as described below under "Tmmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", and infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious Disease."). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indication is include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, hemophilia, hypercoagulation, diabetes mellitus. A highly preferred indication is diabetes mellitus. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic neuropathy, kidney disease (e.g., renal failure, neptropathy, nerve diseases and disorders as ection below, diabetic neuropathy, herve diseases and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the
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endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. So weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the
assays disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al., Biochem Mol Biol Int, 39(6):1229-36 (1996); Krautheim, A., et al., Br J Pharmacol, 129(4):687-94 (2000); Chandra J, et al., Diabetes, 50 Suppl 1:S44-7 (2001); Suk K, et al., J Immunol, 166(7):4481-9 (2001); Tejedo J, et al., FEBS Lett, 459(2):238-43 (1999); Zhang, S., et al., FEBS Lett, 455(3):315-20 (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1980 777:3519.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	Endothelial Cell Apoptosis
	644
	HE6FV29
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agonists or antagonists of the invention) to	invention includes a method for stimulating endothelial	
promote caspase protease-mediated	cell proliferation. An alternative highly preferred	
apoptosis. Induction of apoptosis in	metho	
endothelial cells supporting the vasculature	inhibiting endothelial cell proliferation. A highly	
of tumors is associated with tumor	preferred embodiment of the invention includes a method	
regression due to loss of tumor blood	for stimulating apoptosis of endothelial cells. An	
supply. Exemplary assays for caspase	alternative highly preferred embodiment of the invention	
apoptosis that may be used or routinely	1g (e.g	
modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred	
of polypeptides of the invention (including	embodiment of the invention includes a method for	
antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred	
the invention) include the assays disclosed	embodiment of the invention includes a method for	
in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred	
 (2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for	
218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly	
 Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method	
the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred	_
incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described	
Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and	
according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,	
available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,	
sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular	
may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular	
include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac	
(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic	
endothelial cells which line blood vessels	overload, and/or as described below under	
and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications	
but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic	
vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such	
 immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels	
	themselves, such as of the arteries, capillaries, veins and/or	
	lymphatics). Highly preferred are indications that	
	stimulate angiogenesis and/or cardiovascularization.	
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	and/or cardiovascularization. Highly preferred	
	indications include antiangiogenic activity to treat solid	
	tullors, icurcillias, and maposis sarcollia, and iculial	_

disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, concurary artery disease, inflammatory vasculitides.	Reynaud's disease and Reynaud's phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as	acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic
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					lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
130	HE6FV29	644	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agomsts or antagomsts of the invention) to mobilize calcium. For	nepuropathy and/or other diseases and disorders as described in the "Renal Disorders" section below). diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	tunne
				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
	-			3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	cations
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	

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			modified to test immunomodulatory	Other preferred indications include benign dysproliferative
			activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, tor
			(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
			antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
			example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
			(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
			practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
			(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
			77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
			Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
			Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
			321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
			are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
			entirety. Human T cells that may be used	described below under "Infectious Disease").
			according to these assays may be isolated	
			using techniques disclosed herein or	
			otherwise known in the art. Human T cells	
			are primary human lymphocytes that	
			mature in the thymus and express a T Cell	
			receptor and CD3, CD4, or CD8. These	
			cells mediate humoral or cell-mediated	
			imminity and may be preactivated to	
			initiality and may be preactivated to	
			enhance responsiveness to	
+			immunomodulatory factors.	
132 HE8FC45	040	Upregulation of CD152	CD152 FMA1. CD152 (a.K.a. C1LA-4)	A nigniy preferred embodiment of the invention
		and activation of T cells	expression is restricted to activated I cells.	includes a method for activating 1 cells. An alternative
			CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
			proliferation. Reduced CD152 expression	tor
			has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
			autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
			CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
			immunoresponses. Assays for	of the invention includes a method for stimulating T cell
			immunomodulatory proteins important in	proliferation. Highly preferred indications include
			the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
			expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
			CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications

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A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia,	endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
A hij An additit associate diabetic r nephropa describec neuropatl diabetic r stroke, in blood ves drowsine coma, car atheroscl stroke, ar	endocrine dis Disorders" se (e.g., diabetic impaired wou diseases and Diseases" se skin), carpal contracture). indication is obesity. Add weight loss o highly prefer with insulin r
Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin	secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1995), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain
Stimulation of insulin secretion from pancreatic beta cells.	
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				characteristics typical of native nancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	
134	HE8FD92	648	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	tunne
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
				(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	

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			cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an	
			X-ray induced rat transplantable	
			insumoma. These cents retain characteristics typical of native pancreatic	
			beta cells including glucose inducible	
			insulin secretion. References: Asfari et al.	
			Endocrinology 1992 130:167.	The state of the s
135 HE8FD92	649	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
		secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
		pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
	·		of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
			antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
			the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
			secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
			is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
			insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
	-		pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
			glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
-			proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
			key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
			assays that may be used or routinely	stroke, and other diseases and disorders as described in the
			modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
			secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
			polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
			antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
			the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
			Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
			2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
			Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
			Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
			(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
		•	Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
			(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
			herein incorporated by reference in its	highly preferred indications are complications associated
			entirety. Pancreatic cells that may be used	with insulin resistance.
			according to these assays are publicly	

				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
	-			X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
136	HE8FD92	650	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include

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		•	herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	weight loss of alternatively, weight gain. highly preferred indications are complications associated with insulin resistance.
137 HE8FD92	651	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious

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skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.
	Production of ICAM-1
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				Cells that may be used according to these	
				assays are publicly available (e.g., through	
				the AICC) and/or may be routinely	
				generated. Exemplary cents that may be	
				used according to these assays include Aortic Smooth Muscle Cells (AOSMC):	
				such as bovine AOSMC.	
139	HE8TY46	653	Activation of	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			Hepatocyte ERK	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating hepatocyte cell
			Signaling Pathway	transduction that regulate cell proliferation	proliferation. An alternative highly preferred embodiment
				or differentiation are well known in the art	of the invention includes a method for inhibiting
				and may be used or routinely modified to	hepatocyte cell proliferation. A highly preferred
				assess the ability of polypeptides of the	embodiment of the invention includes a method for
				invention (including antibodies and	stimulating hepatocyte cell differentiation. An alternative
				agonists or antagonists of the invention) to	highly preferred embodiment of the invention includes a
				promote or inhibit cell proliferation,	method for inhibiting hepatocyte cell differentiation. A
				activation, and differentiation. Exemplary	highly preferred embodiment of the invention includes a
				assays for ERK kinase activity that may be	method for activating hepatocyte cells. An alternative
				used or routinely modified to test ERK	highly preferred embodiment of the invention includes a
				kinase-induced activity of polypeptides of	method for inhibiting the activation of and/or inactivating
				the invention (including antibodies and	hepatocyte cells. Highly preferred indications include
				agonists or antagonists of the invention)	disorders of the liver and/or endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Preferred indications include neoplastic diseases (e.g., as
				(1998); Kyriakis JM, Biochem Soc Symp	described below under "Hyperproliferative Disorders"),
				64:29-48 (1999); Chang and Karin, Nature	blood disorders (e.g., as described below under "Immune
				410(6824):37-40 (2001); and Cobb MH,	Activity", "Cardiovascular Disorders", and/or "Blood-
				Prog Biophys Mol Biol 71(3-4):479-500	Related Disorders"), immune disorders (e.g., as described
				(1999); the contents of each of which are	below under "Immune Activity"), neural disorders (e.g., as
				herein incorporated by reference in its	described below under "Neural Activity and Neurological
				entirety. Rat liver hepatoma cells that may	Diseases"), and infection (e.g., as described below under
				be used according to these assays are	"Infectious Disease"). A highly preferred
				publicly available (e.g., through the	indication is diabetes mellitus. An additional highly
				ATCC). Exemplary rat liver hepatoma	preferred indication is a complication associated with
				cells that may be used according to these	diabetes (e.g., diabetic retinopathy, diabetic nephropathy,
				assays include H4lle cells, which are	kidney disease (e.g., renal failure, nephropathy and/or
				known to respond to glucocorticoids,	other diseases and disorders as described in the "Renal

insulin or cAMP derivatives.	Disorders" section below), diabetic neuropathy, nerve
	disease and nerve damage (e.g., due to diabetic
	neuropathy), blood vessel blockage, heart disease, stroke,
	impotence (e.g., due to diabetic neuropathy or blood vessel
	blockage), seizures, mental confusion, drowsiness,
	nonketotic hyperglycemic-hyperosmolar coma,
	cardiovascular disease (e.g., heart disease, atherosclerosis,
	microvascular disease, hypertension, stroke, and other
	diseases and disorders as described in the "Cardiovascular
	Disorders" section below), dyslipidemia, endocrine
	disorders (as described in the "Endocrine Disorders"
	section below), neuropathy, vision impairment (e.g.,
	diabetic retinopathy and blindness), ulcers and impaired
	wound healing, infection (e.g., infectious diseases and
	disorders as described in the "Infectious Diseases" section
	below, especially of the urinary tract and skin), carpal
	tunnel syndrome and Dupuytren's contracture). An
	additional highly preferred indication is obesity and/or
	complications associated with obesity. Additional highly
	preferred indications include weight loss or alternatively,
	weight gain. Additional highly preferred indications
	are complications associated with insulin resistance.
	Additional highly preferred indications are disorders of the
	musculoskeletal systems including myopathies, muscular
	dystrophy, and/or as described herein.
	Additional highly preferred indications include, hepatitis,
	jaundice, gallstones, cirrhosis of the liver, degenerative or
	necrotic liver disease, alcoholic liver diseases, fibrosis,
	liver regeneration, metabolic disease, dyslipidemia and
	chlolesterol metabolism. Additional highly
	preferred indications include neoplasms and cancers, such
	as, hepatocarcinomas, other liver cancers, and colon and
	pancreatic cancer. Preferred indications also include
	prostate, breast, lung, esophageal, stomach, brain, and
	urinary cancer. Other preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or

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					dysplasia.
140	HE9CY05	654	Activation of	Assays for the activation of transcription	A highly preferred indication includes allergy. A
			transcription through	through the GATA3 response element are	highly preferred indication includes asthma. A highly
			GATA-3 response	well-known in the art and may be used or	preferred indication includes rhinitis. Additional highly
			element in immune	routinely modified to assess the ability of	preferred indications include infection (e.g., an infectious
			cells (such as T-cells).	polypeptides of the invention (including	disease as described below under "Infectious Disease"),
				antibodies and agonists or antagonists of	and inflammation and inflammatory disorders.
				the invention) to regulate GATA3	Preferred indications include blood disorders (e.g., as
				transcription factors and modulate	described below under "Immune Activity", "Blood-
				expression of genes important for Th2	Related Disorders", and/or "Cardiovascular Disorders").
				immune response development.	Preferred indications include autoimmune diseases (e.g.,
				Exemplary assays for transcription through	rheumatoid arthritis, systemic lupus erythematosis,
				the GATA3 response element that may be	multiple sclerosis and/or as described below) and
				used or routinely modified to test GATA3-	immunodeficiencies (e.g., as described below).
				response element activity of polypeptides	Preferred indications include neoplastic diseases (e.g.,
				of the invention (including antibodies and	leukemia, lymphoma, melanoma, and/or as described
				agonists or antagonists of the invention)	below under "Hyperproliferative Disorders"). Preferred
				include assays disclosed in Berger et al.,	indications include neoplasms and cancer, such as, for
				Gene 66:1-10 (1998); Cullen and Malm,	example, leukemia, lymphoma, melanoma, and prostate,
				Methods in Enzymol 216:362-368 (1992);	breast, lung, colon, pancreatic, esophageal, stomach,
				Henthorn et al., Proc Natl Acad Sci USA	brain, liver and urinary cancer. Other preferred indications
				85:6342-6346 (1988); Flavell et al., Cold	include benign dysproliferative disorders and pre-
				Spring Harb Symp Quant Biol 64:563-571	neoplastic conditions, such as, for example, hyperplasia,
				(1999); Rodriguez-Palmero et al., Eur J	metaplasia, and/or dysplasia. Preferred indications
				Immunol 29(12):3914-3924 (1999); Zheng	include anemia, pancytopenia, leukopenia,
				and Flavell, Cell 89(4):587-596 (1997);	thrombocytopenia, leukemias, Hodgkin's disease, acute
				and Henderson et al., Mol Cell Biol	lymphocytic anemia (ALL), plasmacytomas, multiple
				14(6):4286-4294 (1994), the contents of	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				each of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
				reference in its entirety. T cells that may	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				be used according to these assays are	immune reactions to transplanted organs and tissues,
				publicly available (e.g., through the	hemophilia, hypercoagulation, diabetes mellitus,
				ATCC). Exemplary mouse T cells that	endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays	
				include the HT2 cell line, which is a	
		-		suspension culture of IL-2 dependent T	
				cells that also respond to IL-4.	

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141	HE9EA10	655	Regulation of viability	Assays for the regulation of viability and	A highly preferred indication is diabetes mellitus.
			and proliferation of	proliferation of cells in vitro are well-	An additional highly preferred indication is a complication
			pancreatic beta cells.	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
				routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
				polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
-				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
·				the invention) to regulate viability and	neuropathy, nerve disease and nerve damage (e.g., due to
				proliferation of pancreatic beta cells. For	diabetic neuropathy), blood vessel blockage, heart disease,
				example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
				viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
				regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
				invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
				agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
				include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
				BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
				(2001); Huotari MA, et al., Endocrinology,	skin), carpal tunnel syndrome and Dupuytren's
•				139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
				Biol Chem 1998 Jul 10;273(28):17771-9	indication is obesity and/or complications associated with
				(1998), the contents of each of which is	obesity. Additional highly preferred indications include
				herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
			-	entirety. Pancreatic cells that may be used	highly preferred indications are complications associated
				according to these assays are publicly	with insulin resistance.
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	

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				beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	
	HE9GG20	929	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
143	HEBCI18	657	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription that may be used or	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemiclupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").

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				routinely modified to test NFAT-response	Preferred indications include neonlastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
			-	Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
	•••			Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.
				ATCC). Exemplary human T cells that	
				may be used according to these assays	
				include the SUPT cell line, which is a	
				suspension culture of IL-2 and IL-4	
				responsive T cells.	
144	HEBCY54	658	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription through	through the FAS promoter element are	An additional highly preferred indication is a complication
			the FAS promoter	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			element in hepatocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
				polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to activate the FAS	neuropathy, nerve disease and nerve damage (e.g., due to
				promoter element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
				and to regulate transcription of FAS, a key	stroke, impotence (e.g., due to diabetic neuropathy or
				enzyme for lipogenesis. FAS promoter is	blood vessel blockage), seizures, mental confusion,
				regulated by many transcription factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				including SREBP. Insulin increases FAS	coma, cardiovascular disease (e.g., heart disease,
				gene transcription in livers of diabetic	atherosclerosis, microvascular disease, hypertension,

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				mice. This stimulation of transcription is	stroke, and other diseases and disorders as described in the
				also somewhat glucose dependent.	"Cardiovascular Disorders" section below), dyslipidemia,
				Exemplary assays that may be used or	endocrine disorders (as described in the "Endocrine
				routinely modified to test for FAS	Disorders" section below), neuropathy, vision impairment
				promoter element activity (in hepatocytes)	(e.g., diabetic retinopathy and blindness), ulcers and
				by polypeptides of the invention (including	impaired wound healing, and infection (e.g., infectious
				antibodies and agonists or antagonists of	diseases and disorders as described in the "Infectious"
				the invention) include assays disclosed in	Diseases" section below, especially of the urinary tract and
				Xiong, S., et al., Proc Natl Acad Sci	skin), carpal tunnel syndrome and Dupuytren's
				U.S.A., 97(8):3948-53 (2000); Roder, K.,	contracture). An additional highly preferred
				et al., Eur J Biochem, 260(3):743-51	indication is obesity and/or complications associated with
				(1999); Oskouian B, et al., Biochem J, 317	obesity. Additional highly preferred indications include
				(Pt 1):257-65 (1996); Berger, et al., Gene	weight loss or alternatively, weight gain. Aditional
				66:1-10 (1988); and, Cullen, B., et al.,	highly preferred indications are complications associated
				Methods in Enzymol. 216:362–368 (1992),	with insulin resistance.
				the contents of each of which is herein	
				incorporated by reference in its entirety.	
				Hepatocytes that may be used according to	
				these assays, such as H4IIE cells, are	
				publicly available (e.g., through the	
				ATCC) and/or may be routinely generated.	
				Exemplary hepatocytes that may be used	
				according to these assays include rat liver	
				hepatoma cell line(s) inducible with	
				glucocorticoids, insulin, or cAMP	
				derivatives.	
145	HEBDF77	629	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies

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				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications include inflammation and inflammatory disorders and
				agonists of antagonists of the invention) include assays disclosed in Berger et al.,	include initialination and initialinitatory disoluters, and treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
	•			Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
	•			content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
-				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
•••					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
-					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
+					under "Infectious Disease").
146 HEB	HEBDQ91	099	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications

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				the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, hyperplasia, metaplasia, and/or dysplasia. Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
146	невроој	099	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a

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 antibodies and agonists or antagonists of	method for activating T cells. An alternative highly
the invention) to stimulate IL-2 expression	preferred embodiment of the invention includes a method
 in T cells. Exemplary assays for	for inhibiting the activation of and/or inactivating T cells.
transcription through the CD28 response	A highly preferred embodiment of the invention includes a
element that may be used or routinely	method for stimulating (e.g., increasing) IL-2 production.
 modified to test CD28-response element	An alternative highly preferred embodiment of the
 activity of polypeptides of the invention	invention includes a method for inhibiting (e.g., reducing)
(including antibodies and agonists or	IL-2 production. Additional highly preferred
antagonists of the invention) include	indications include inflammation and inflammatory
assays disclosed in Berger et al., Gene	disorders. Highly preferred indications include
 66:1-10 (1998); Cullen and Malm,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. Highly
(1997); Parra et al., J Immunol	preferred indications include neoplastic diseases (e.g.,
166(4):2437-2443 (2001); and Butscher et	melanoma, renal cell carcinoma, leukemia, lymphoma,
al., J Biol Chem 3(1):552-560 (1998), the	and/or as described below under "Hyperproliferative
 contents of each of which are herein	Disorders"). Highly preferred indications include
incorporated by reference in its entirety. T	neoplasms and cancers, such as, for example, melanoma
cells that may be used according to these	(e.g., metastatic melanoma), renal cell carcinoma (e.g.,
assays are publicly available (e.g., through	metastatic renal cell carcinoma), leukemia, lymphoma
the ATCC). Exemplary human T cells that	(e.g., T cell lymphoma), and prostate, breast, lung, colon,
may be used according to these assays	pancreatic, esophageal, stomach, brain, liver and urinary
include the SUPT cell line, which is a	cancer. Other preferred indications include benign
suspension culture of IL-2 and IL-4	dysproliferative disorders and pre-neoplastic conditions,
responsive T cells.	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia. A highly preferred indication includes
	infection (e.g., AIDS, tuberculosis, infections associated
	with granulomatous disease, and osteoporosis, and/or as
	described below under "Infectious Disease"). A highly
	preferred indication is AIDS. Additional highly preferred
	indications include suppression of immune reactions to
	transplanted organs and/or tissues, uveitis, psoriasis, and
	tropical spastic paraparesis. Preferred indications
	include blood disorders (e.g., as described below under
	"Immune Activity", "Blood-Related Disorders", and/or

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				"Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
147 HEBFR46	661	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated highly preferred indications are complications associated highly preferred indications are complications associated

			available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	
147 HEBFR46	661	Activation of transcription through API response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,

			incorporated by reference in its entirety. Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is an IL-2 and IL-4 responsive suspension-	anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
147 HEBFR46	961	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 160(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cells. An alternative highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for stimulating the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) LL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) LL-2 production. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include response, and suppressing a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma (e.g., metastatic renal cell carcinoma). Leukemia, lymphoma
			the ATCC). Exemplary human T cells that may be used according to these assays	(e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary

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				include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
147	HEBFR46	661	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under

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				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.
			٠	ATCC). Exemplary human T cells that	
				may be used according to these assays	
				include the SUPT cell line, which is a	
			-	suspension culture of IL-2 and IL-4	
				responsive T cells.	
147	HEBFR46	199	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy.
			transcription through	through the Signal Transducers and	Another highly preferred indication is asthma.
			STAT6 response	Activators of Transcription (STAT6)	Additional highly preferred indications include
			element in immune	response element are well-known in the art	inflammation and inflammatory disorders.
			cells (such as T-cells).	and may be used or routinely modified to	Preferred indications include blood disorders (e.g., as
				assess the ability of polypeptides of the	described below under "Immune Activity", "Blood-
				invention (including antibodies and	Related Disorders", and/or "Cardiovascular Disorders").
				agonists or antagonists of the invention) to	Preferred indications include autoimmune diseases (e.g.,
•				regulate STAT6 transcription factors and	rheumatoid arthritis, systemic lupus erythematosis,
				modulate the expression of multiple genes.	multiple sclerosis and/or as described below) and
				Exemplary assays for transcription through	immunodeficiencies (e.g., as described below).
				the STAT6 response element that may be	Preferred indications include neoplastic diseases (e.g.,
				used or routinely modified to test STAT6	leukemia, lymphoma, melanoma, and/or as described
				response element activity of the	below under "Hyperproliferative Disorders"). Preferred
				polypeptides of the invention (including	indications include neoplasms and cancers, such as,

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147	HEBFR46	661	Activation of transcription through NFKB response	antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or portively modified to assess the ability of	leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, Preferred indications include anemia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infectiou Disease. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Inneuro Activiva" "Rlood-Related Disorders" and/or
			cells (such as T-cells).	polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	"Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal,

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				Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and
				85:6342-6346 (1988); Black et al., Virus	pre-neoplastic conditions, such as, for example,
				ones 13(2):103-11/ (1997); and riaser et al., 29(3):838-844 (1999), the contents of	nyperpiasia, metapiasia, angroi dyspiasia. Preferred indications also include anemia, pancytopenia, leukopenia,
				each of which are herein incorporated by	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				reference in its entirety. T cells that may	anemia (ALL), plasmacytomas, multiple myeloma,
				be used according to these assays are	Burkitt's lymphoma, arthritis, AIDS, granulomatous
		`		publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia,
				AICC). Exemplary numan 1 cells that	neuropmila, psonasis, nemopnilla, nypercoagulation, dispetes mellinis endocarditis meningitis I vme Disease
				inay of used according to these assays include the SUPT cell line, which is a	diabetes inclinus, elitocalulus, inclinigius, Lynie Disease, suppression of immine reactions to transplanted organs.
				suspension culture of IL-2 and IL-4	asthma and allergy.
				responsive T cells.	
148	HEBGE07	799	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
		· · · ·		antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic

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			Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.	granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
148 HEBGE07	995	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with

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			136(10):4589-601 (1995);Mogami H, et al., Endocrinology, 136(7):2960-6 (1995);	tion t
			Alconardson 5.5, et al., blochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al.,	contracture). An additional highly preferred indication is obesity and/or complications associated with
_			Cell Calcium 1989 Nov-Dec;10(8):535-41	cations i
			(1989), the contents of each of which is herein incompared by reference in its	weight loss or alternatively, weight gain. Aditional
			entirety. Pancreatic cells that may be used	with insulin resistance.
			according to these assays are publicly	
			available (e.g., through the ATCC) and/or	
			may be routinely generated. Exemplary	
			according to these assays include HTTT15	
			Cells. HITT15 are an adherent epithelial	
-			cell line established from Syrian hamster	
			islet cells transformed with SV40. These	
			cells express glucagon, somatostatin, and	
			glucocorticoid receptors. The cells secrete	
			insulin, which is stimulated by glucose and	
			glucagon and suppressed by somatostatin	
			or glucocorticoids. ATTC# CRL-1777	
			Refs: Lord and Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc. Natl. Acad.	
\dashv			Sci. USA 78: 4339-4343, 1981.	
150 HELAT35	664	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
			and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
			participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
			and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
			role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
			cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
			of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
			disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
			chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
			Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
			differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
			a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
			expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,

				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
151	HELBU54	999	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune

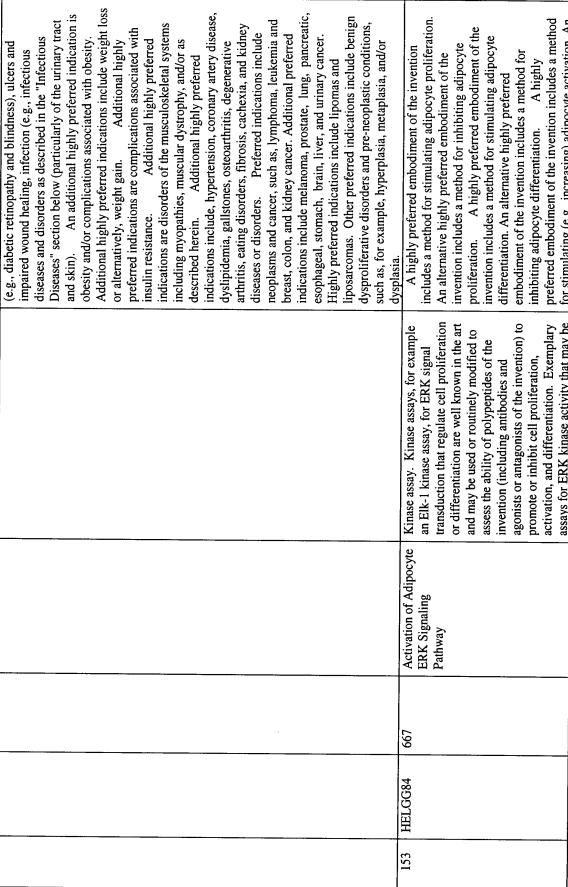
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Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under	indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thromboottonia, Hodokin's disease assite lumphoottonia.	anemia (ALL), plasmacytomas, multiple myeloma, anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for
routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include	66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the	incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to
in immune cells (such as T-cells).			Activation of Adipocyte ERK Signaling Pathway
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		·	HELGG84
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promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
activation, and differentiation. Exemplary	on ii
assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
 agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
 (1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
 include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
 differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment

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dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An
	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be
	Activation of Adipocyte ERK Signaling Pathway





	used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
	kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
	the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
-	agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
	include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
	al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
	(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
	Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
	(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
	64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
	410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
	Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders".
	(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
	herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
	entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
	be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
	publicly available (e.g., through the	described below under "Infectious Disease").
	ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus An
	that may be used according to these assays	ation
	include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinonathy
	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure.
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease.
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders' section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing infection (c.g., infections)
		diseases and disorders as described in the "Infectious"

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Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones
	Production of IL-6
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	highly preferred indications include inflammation and inflammatory disorders.	response element are well-known in the art	element in immune	
	highly preferred indication is asthma. Additional	through the Signal Transducers and	transcription through	
		Assays for the activation of transmission	Activation of	699
		cytokines, initiate and upregulate T cell		
		which, when activated by antigen and/or		
		presenting cells in suspension culture,		
		art. Human dendritic cells are antigen		
	described below under "Infectious Disease").	disclosed herein or otherwise known in the		
	infe	assays may be isolated using techniques		
	meningitis, and Lyme Disease. An additional preferred	cells that may be used according to these		
	hypercoagulation, diabetes mellitus, endocarditis,	reference in its entirety. Human dendritic		
	transplanted organs and tissues, hemophilia,	each of which are herein incorporated by		
	neutrophilia, psoriasis, suppression of immune reactions to	158:2919-2925 (1997), the contents of		
	inflammatory bowel disease, sepsis, neutropenia.	(2000); and Verhasselt et al., J Immunol		
	Iymphoma, arthritis, AIDS, granulomatous disease	a practical approach" Chapter 6:138-160		
	lymphocytic anemia (ALL), multiple myeloma. Burkitt's	204(1999); Rowland et al., "Lymphocytes:		
	leukopenia, thrombocytopenia, Hodgkin's disease, acute	J Biomolecular Screening 4:193-		
	Preferred indications include anemia, pancytopenia.	include assays disclosed in Miraglia et al.,		
	example, hyperplasia, metaplasia, and/or dysplasia.	agonists or antagonists of the invention)		
	disorders and pre-neoplastic conditions, such as, for	the invention (including antibodies and		
	Other preferred indications include benign dysproliferative	diffferentiation activity of polypeptides of		
_	esophageal, stomach, brain, liver and urinary cancer.	modified to test immunomodulatory and		
	melanoma, and prostate, breast, lung, colon, nancreatic	Such assays that may be used or routinely		
	as, myeloma, plasmacytoma, leukemia, lymphoma.	proliferation and functional activities.		
	preferred indications include neoplasms and cancers, such	the stimulation and upregulation of T cell		
	below under "Hyperproliferative Disorders") Highly	production of cytokines, such as IL-6, and		
	leukemia, lymphoma, melanoma, and/or as described	immunomodulatory proteins evaluate the		
_	neoplastic diseases (e.g., myeloma, plasmacytoma,	Exemplary assays that test for		
	asthma and allergy. Highly preferred indications include	modulate T cell proliferation and function.		
	disorders. Additional highly preferred indications include	immunomodulation and differentiation and		
	indications include inflammation and inflammatory	the invention) to mediate	-	
	b B	antibodies and agonists or antagonists of		
	mediated immune response and alternatively suppressing a	of polypeptides of the invention (including		
	preferred indications also include boosting a B cell-	or routinely modified to assess the ability	•	
	immunodeficiencies (e.g., as described below). Highly	are well known in the art and may be used		

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include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below).	Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. Additional preferred indications include infectious disease as described below under "Infectious Disease").	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Diseases").
and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes.	Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen	and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of
cells (such as natural killer cells).			Activation of transcription through AP1 response element in immune cells (such as T-cells).
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			HEPBA14
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				the invention) to modulate growth and	Highly preferred indications include autoimmine diseases
	-			other cell functions Dynamical control for	(a) The control of th
				outel cell functions. Exemplary assays for	(e.g., meumatoid armitis, systemic lupus erytnematosis,
				transcription through the AP1 response	multiple sclerosis and/or as described below) and
		-		element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
		<:		assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis.
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
			•	may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
				with cytotoxic activity.	
157	HEQAH80	671	Activation of Natural	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			Killer Cell ERK	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating natural killer cell
			Signaling Pathway.	transduction that regulate cell proliferation	proliferation. An alternative highly preferred embodiment
				or differentiation are well known in the art	of the invention includes a method for inhibiting natural
				and may be used or routinely modified to	killer cell proliferation. A highly preferred
		·····		assess the ability of polypeptides of the	embodiment of the invention includes a method for
				invention (including antibodies and	stimulating natural killer cell differentiation. An
				agonists or antagonists of the invention) to	alternative highly preferred embodiment of the invention
				promote or inhibit cell proliferation,	includes a method for inhibiting natural killer cell
				activation, and differentiation. Exemplary	differentiation. Highly preferred indications include
				assays for ERK kinase activity that may be	neoplastic diseases (e.g., as described below under

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			used or routinely modified to test FRK	"Hyperproliferative Disorders") blood disorders (e.g. as
			kinase-induced activity of polypeptides of	described below under "Immune Activity",
			the invention (including antibodies and	"Cardiovascular Disorders", and/or "Blood-Related
			agonists or antagonists of the invention)	Disorders"), immune disorders (e.g., as described below
			include the assays disclosed in Forrer et	under "Immune Activity") and infections (e.g., as
			al., Biol Chem 379(8-9):1101-1110	described below under "Infectious Disease"). Preferred
			(1998); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., as described
			64:29-48 (1999); Chang and Karin, Nature	below under "Immune Activity", "Blood-Related
			410(6824):37-40 (2001); and Cobb MH,	Disorders", and/or "Cardiovascular Disorders"). Highly
			Prog Biophys Mol Biol 71(3-4):479-500	preferred indications include autoimmune diseases (e.g.,
			(1999); the contents of each of which are	rheumatoid arthritis, systemic lupus erythematosis,
			herein incorporated by reference in its	multiple sclerosis and/or as described below) and
	-		entirety. Natural killer cells that may be	immunodeficiencies (e.g., as described below). Additional
			used according to these assays are publicly	highly preferred indications include inflammation and
			available (e.g., through the ATCC).	inflammatory disorders. Highly preferred indications
			Exemplary natural killer cells that may be	ı as, l
			used according to these assays include the	breast, lung, colon, pancreatic, esophageal, stomach,
			human natural killer cell lines (for	brain, liver, urinary cancer, lymphoma and leukemias.
			example, NK-YT cells which have	Other preferred indications include benign dysproliferative
			cytolytic and cytotoxic activity) or primary	disorders and pre-neoplastic conditions, such as, for
			NK cells.	example, hyperplasia, metaplasia, and/or dysplasia.
				Other highly preferred indications include, pancytopenia,
				leukopenia, leukemias, Hodgkin's disease, acute
				lymphocytic anemia (ALL), arthritis, asthma, AIDS,
				granulomatous disease, inflammatory bowel disease,
				sepsis, psoriasis, immune reactions to transplanted organs
				and tissues, endocarditis, meningitis, Lyme Disease, and
+				allergies.
IS8 HEQBF89	672	Activation of	Kinase assay. JNK and p38 kinase assays	A highly preferred embodiment of the invention
		Endothelial Cell p38 or	for signal transduction that regulate cell	includes a method for stimulating endothelial cell growth.
		JNK Signaling	proliferation, activation, or apoptosis are	An alternative highly preferred embodiment of the
		Pathway.	well known in the art and may be used or	invention includes a method for inhibiting endothelial cell
			routinely modified to assess the ability of	growth. A highly preferred embodiment of the
			polypeptides of the invention (including	invention includes a method for stimulating endothelial
			antibodies and agonists or antagonists of	cell proliferation. An alternative highly preferred
			the invention) to promote or inhibit cell	embodiment of the invention includes a method for
			proliferation, activation, and apoptosis.	inhibiting endothelial cell proliferation. A highly

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	indications include antiangiogenic activity to treat solid timore leukemiae and Rancel's carcoma and ratinal	disorders. Highly preferred indications include neoplasms	and cancer, such as, Kaposi's sarcoma, hemangioma	(capillary and cavernous), glomus tumors, telangiectasia,	bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary	cancer. Preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions,	such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Highly preferred indications also include	arterial disease, such as, atherosclerosis, hypertension,	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	aneurysms, restenosis; venous and lymphatic disorders	such as thrombophlebitis, lymphangitis, and lymphedema;	and other vascular disorders such as peripheral vascular	disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	(e.g., vascular injury such as, injury resulting from balloon	angioplasty, and atheroschlerotic lesions), implant	fixation, scarring, ischemia reperfusion injury, rheumatoid	arthritis, cerebrovascular disease, renal diseases such as	acute renal failure, and osteoporosis. Additional highly	preferred indications include stroke, graft rejection,	diabetic or other retinopathies, thrombotic and coagulative	disorders, vascularitis, lymph angiogenesis, sexual	disorders, age-related macular degeneration, and treatment	/prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas,	heart disease, cardiac arrest, heart valve disease, and	vascular disease. Preferred indications include blood	disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or
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					"Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
159 HETC116	7116	673	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are berein incorporated by reference in its	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Preferred indications include endocrine Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders", immune disorders and/or and disorders and/or and discorders and/or and disorders and/or and disorders and/or and discorders and/or and disorders and/or and disorders and/or and discorders and/or and discorders and/or and disorders and/or and discorders and/o
				entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells	disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under "Theories Disease"). A highly preferred indication is diabetes mellitus. An

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additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic	neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis microvascular disease hymertension	stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious	Diseases' section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disordered of the musculoskeleral extends.	including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer.
that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation	and undergo a pre-adipocyte to adipose- like conversion under appropriate differentiation conditions known in the art.			

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Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indications is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include asthma and allergy. Highly preferred indications include asthma and allergy. Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention). Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraelia et al.
	Production of IL-6
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				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
			•	disclosed herein or otherwise known in the	described below under "Infectious Disease").
•				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	2
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
160	HETDW58	674	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that are	includes a method for stimulating (e.g., increasing) MCP-1
				produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
				to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
				monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as
		-		modified to assess the ability of	described below under "Infectious Disease"). Additional
				polypeptides of the invention (including	highly preferred indications include inflammation and
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
		•		the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
-				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs

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				antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis (bacterial and viral), Lyme Disease, asthma, and allergy Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
161	HETEY67	675	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred embodiment of indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred

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			the invention) to mediate	indications include inflammation and inflammatory
			immunomodulation and differentiation and	disorders. Additional highly preferred indications include
			modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
			Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
			immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
			production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
			the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
			proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
			Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
			modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
			diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
			the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
			agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
			include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia.
			J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
			a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease.
			(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia
			158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
			each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
			reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
			cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
			assays may be isolated using techniques	£
			disclosed herein or otherwise known in the	described below under "Infectious Disease").
			art. Human dendritic cells are antigen	
			presenting cells in suspension culture,	
			which, when activated by antigen and/or	
			cytokines, initiate and upregulate T cell	
			proliferation and functional activities.	
162 HFCDW95 (9/9	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
-		transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
		cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders").
		element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
		cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
			antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
			the invention) to increase cAMP, bind to	arthritis, systemic lupus erythematosis, multiple sclerosis
			CREB transcription factor, and modulate	and/or as described below), immunodeficiencies (e.g., as

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			expression of genes involved in a wide	described below), boosting a T cell-mediated immune
			variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
			assays for transcription through the cAMP	response. Additional preferred indications include
			response element that may be used or	inflammation and inflammatory disorders. Highly
			routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
			element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
	w.		invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
			agonists or antagonists of the invention)	indications include neoplasms and cancers, such as,
			include assays disclosed in Berger et al.,	leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's
			Gene 66:1-10 (1998); Cullen and Malm,	lymphoma, non-Hodgkins lymphoma, Hodgkin's disease),
			Methods in Enzymol 216:362-368 (1992);	melanoma, and prostate, breast, lung, colon, pancreatic,
			Henthorn et al., Proc Natl Acad Sci USA	esophageal, stomach, brain, liver and urinary cancer.
		•	85:6342-6346 (1988); Black et al., Virus	Other preferred indications include benign dysproliferative
			Genes 15(2):105-117 (1997); and	disorders and pre-neoplastic conditions, such as, for
			Belkowski et al., J Immunol 161(2):659-	example, hyperplasia, metaplasia, and/or dysplasia.
			665 (1998), the contents of each of which	Preferred indications include anemia, pancytopenia,
			are herein incorporated by reference in its	leukopenia, thrombocytopenia, acute lymphocytic anemia
			entirety. T cells that may be used	(ALL), plasmacytomas, multiple myeloma, arthritis,
			according to these assays are publicly	AIDS, granulomatous disease, inflammatory bowel
			available (e.g., through the ATCC).	disease, sepsis, neutropenia, neutrophilia, psoriasis,
-	7.00		Exemplary human T cells that may be used	suppression of immune reactions to transplanted organs
			according to these assays include the	and tissues, hemophilia, hypercoagulation, diabetes
			JURKAT cell line, which is a suspension	mellitus, endocarditis, meningitis, Lyme Disease, and
			culture of leukemia cells that produce IL-2	asthma and allergy.
+			when stimulated.	
162 HFCDW95	929	Activation of	Assays for the activation of transcription	Highly preferred indications include inflammation and
		transcription through	through the NFKB response element are	inflammatory disorders. Highly preferred indications
		NFKB response	well-known in the art and may be used or	include blood disorders (e.g., as described below under
		element in immune	routinely modified to assess the ability of	"Immune Activity", "Blood-Related Disorders", and/or
		cells (such as T-cells).	polypeptides of the invention (including	"Cardiovascular Disorders"). Highly preferred indications
			antibodies and agonists or antagonists of	include autoimmune diseases (e.g., rheumatoid arthritis,
			the invention) to regulate NFKB	systemic lupus erythematosis, multiple sclerosis and/or as
			transcription factors and modulate	described below), and immunodeficiencies (e.g., as
			expression of immunomodulatory genes.	described below). An additional highly preferred
			Exemplary assays for transcription through	indication is infection (e.g., AIDS, and/or an infectious
			the NFKB response element that may be	disease as described below under "Infectious Disease").
			used or rountinely modified to test NFKB-	Highly preferred indications include neoplastic diseases

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				test for DMEF1 response element activity (in adinocytes and pre-adinocytes) by	diseases and disorders as described in the "Infectious Diseases" section below especially of the urinary tract and
				polypeptides of the invention (including	skin), carpal tunnel syndrome and Dupuytren's
				antibodies and agonists or antagonists of	contracture). An additional highly preferred
				the invention) include assays disclosed	indication is obesity and/or complications associated with
				inThai, M.V., et al., J Biol Chem,	obesity. Additional highly preferred indications include
			,	273(23):14285-92 (1998); Mora, S., et al.,	weight loss or alternatively, weight gain. Aditional
				J Biol Chem, 275(21):16323-8 (2000); Liu,	highly preferred indications are complications associated
				M.L., et al., J Biol Chem, 269(45):28514-	with insulin resistance.
				21 (1994); "Identification of a 30-base pair	
				regulatory element and novel DNA	
				binding protein that regulates the human	
				GLUT4 promoter in transgenic mice", J	
				Biol Chem. 2000 Aug 4;275(31):23666-	
				73; Berger, et al., Gene 66:1-10 (1988);	
				and, Cullen, B., et al., Methods in	
				Enzymol. 216:362–368 (1992), the	
				contents of each of which is herein	
				incorporated by reference in its entirety.	
				Adipocytes and pre-adipocytes that may be	
				used according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				cells that may be used according to these	
				assays include the mouse 3T3-L1 cell line	
				which is an adherent mouse preadipocyte	
				cell line. Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3 fibroblasts	
				developed through clonal isolation. These	
				cells undergo a pre-adipocyte to adipose-	
				like conversion under appropriate	
				differentiation culture conditions.	
164	HFCFD04	8/9	Production of IL-6	L-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	_
-				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred

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cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasma-yomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", http://disorder. Assays for immunomodulatory be used care are and may be used or polypeptides of the invention (including antibodies and agoists or antagonists of the invention of T cell proliferation and direction and functional activities. Such assays that may be used or routinely profileration and functional activities. Such assays that may be used or routinely profileration and functional activities. Such assays that may be used or routinely profileration and functional activities. Such assays disclosed in Miraglia et al., 18 monbecular Screening 4:193- (1909); Rowland et al., "Lymphoryes and persentely approach." Hyperplasia, metaplasia, and/or dysplasia. Indications include and gonists or antagonists of the invention) including antibodies and equipation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activities. Such assays disclosed in Miraglia et al., 1 Immunol (including antibodies and elementar Screening 4:193- (1999); Rowland et al., "Lymphoryes inflammand by a practical using techniques of the wither are brern incorporated by referred indications i	
cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate modulate T cell proliferation and function. Exemplary assays that test for immunomodulation and upregulation of T cell proliferation and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques	of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cyokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention) include assays disclosed in Miraglia et al., J Biomoleculas Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., I Immunol 158:2919-2925 (1997), the contents of each of which are berein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques assays disclosed herein or otherwise known in the
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				art Human dendritic cells are antioen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
		-		cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
165	HFCFE20	629	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			PI3 Kinase Signalling	an GSK-3 assays, for PI3 kinase signal	includes a method for increasing adipocyte survival An
			Pathway	transduction that regulate glucose	alternative highly preferred embodiment of the invention
				metabolism and cell survival are well-	includes a method for decreasing adipocyte survival. A
				known in the art and may be used or	preferred embodiment of the invention includes a method
				routinely modified to assess the ability of	for stimulating adipocyte proliferation. An alternative
				polypeptides of the invention (including	highly preferred embodiment of the invention includes a
				antibodies and agonists or antagonists of	method for inhibiting adipocyte proliferation. A
				the invention) to promote or inhibit	preferred embodiment of the invention includes a method
				glucose metabolism and cell survival.	for stimulating adipocyte differentiation. An alternative
				Exemplary assays for PI3 kinase activity	highly preferred embodiment of the invention includes a
				that may be used or routinely modified to	method for inhibiting adipocyte differentiation. Highly
				test PI3 kinase-induced activity of	LS (C
				polypeptides of the invention (including	described below under "Endocrine Disorders").
				antibodies and agonists or antagonists of	Preferred indications include neoplastic diseases (e.g.,
				the invention) include assays disclosed in	lipomas, liposarcomas, and/or as described below under
				Forrer et al., Biol Chem 379(8-9):1101-	"Hyperproliferative Disorders"), blood disorders (e.g.,
				1110 (1998); Nikoulina et al., Diabetes	hypertension, congestive heart failure, blood vessel
				49(2):263-271 (2000); and Schreyer et al.,	blockage, heart disease, stroke, impotence and/or as
				Diabetes 48(8):1662-1666 (1999), the	described below under "Immune Activity",
				contents of each of which are herein	"Cardiovascular Disorders", and/or "Blood-Related
				incorporated by reference in its entirety.	Disorders"), immune disorders (e.g., as described below
				Mouse adipocyte cells that may be used	under "Immune Activity"), neural disorders (e.g., as
				according to these assays are publicly	described below under "Neural Activity and Neurological
				available (e.g., through the ATCC).	Diseases"), and infection (e.g., as described below under
				Exemplary mouse adipocyte cells that may	"Infectious Disease"). A highly preferred indication
				be used according to these assays include	is diabetes mellitus. An additional highly preferred
				3T3-L1 cells. 3T3-L1 is an adherent	indication is a complication associated with diabetes (e.g.,
				mouse preadipocyte cell line that is a	diabetic retinopathy, diabetic nephropathy, kidney disease
				continous substrain of 3T3 fibroblast cells	(e.g., renal failure, nephropathy and/or other diseases and
				developed through clonal isolation and	disorders as described in the "Renal Disorders" section
				undergo a pre-adipocyte to adipose-like	below), diabetic neuropathy, nerve disease and nerve

conversion under appropriate	damage (e.g, due to diabetic neuropathy), blood vessel
differentiation conditions known in the art.	blockage, heart disease, stroke, impotence (e.g., due to
	diabetic neuropathy or blood vessel blockage), seizures,
	mental confusion, drowsiness, nonketotic hyperglycemic-
	hyperosmolar coma, cardiovascular disease (e.g., neart
	hypertension, stroke, and other diseases and disorders as
	described in the "Cardiovascular Disorders" section
	below), dyslipidemia, endocrine disorders (as described in
	the "Endocrine Disorders" section below), neuropathy,
	vision impairment (e.g., diabetic retinopathy and
	blindness), ulcers and impaired wound healing, infection
	(e.g., infectious diseases and disorders as described in the
	"Infectious Diseases" section below, especially of the
	urinary tract and skin), carpal tunnel syndrome and
	Dupuytren's contracture). An additional highly
	preferred indication is obesity and/or complications
	associated with obesity. Additional highly preferred
	indications include weight loss or alternatively, weight
	gain. Additional highly preferred indications are
	complications associated with insulin resistance.
	Additional highly preferred indications are disorders of the
	musculoskeletal systems including myopathies, muscular
	dystrophy, and/or as described herein.
	Additional highly preferred indications include,
	hypertension, coronary artery disease, dyslipidemia,
	gallstones, osteoarthritis, degenerative arthritis, eating
	disorders, fibrosis, cachexia, and kidney diseases or
	disorders. Highly preferred indications include
	neoplasms and cancer, such as, lipoma, liposarcoma,
	lymphoma, leukemia and breast, colon, and kidney cancer.
	Additional highly preferred indications include melanoma,
	prostate, lung, pancreatic, esophageal, stomach, brain,
	liver, and urinary cancer. Other preferred indications
	include benign dysproliferative disorders and pre-
	neoplastic conditions, such as, for example, hyperplasia,
	metaplasia, and/or dysplasia.

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		stimulate angiogenesis and/or cardiovascularization.
		Highly preferred are indications that inhibit angiogenesis
		and/or cardiovascularization. Highly preferred
		indications include antiangiogenic activity to treat solid
		tumors, leukemias, and Kaposi's sarcoma, and retinal
		disorders. Highly preferred indications include neoplasms
-		and cancer, such as, Kaposi's sarcoma, hemangioma
		(capillary and cavernous), glomus tumors, telangiectasia,
		bacillary angiomatosis, hemangioendothelioma,
		angiosarcoma, haemangiopericytoma, lymphangioma,
		lymphangiosarcoma. Highly preferred indications also
		include cancers such as, prostate, breast, lung, colon,
		pancreatic, esophageal, stomach, brain, liver, and urinary
		cancer. Preferred indications include benign
		dysproliferative disorders and pre-neoplastic conditions,
		such as, for example, hyperplasia, metaplasia, and/or
		dysplasia. Highly preferred indications also include
		arterial disease, such as, atherosclerosis, hypertension,
		coronary artery disease, inflammatory vasculitides,
		Reynaud's disease and Reynaud's phenomenom,
		aneurysms, restenosis; venous and lymphatic disorders
_		such as thrombophlebitis, lymphangitis, and lymphedema;
		and other vascular disorders such as peripheral vascular
		disease, and cancer. Highly preferred indications also
		include trauma such as wounds, burns, and injured tissue
		(e.g., vascular injury such as, injury resulting from balloon
		angioplasty, and atheroschlerotic lesions), implant
		fixation, scarring, ischemia reperfusion injury, rheumatoid
		arthritis, cerebrovascular disease, renal diseases such as
		acute renal failure, and osteoporosis. Additional highly
		graf
		diabetic or other retinopathies, thrombotic and coagulative
		disorders, vascularitis, lymph angiogenesis, sexual
		disorders, age-related macular degeneration, and treatment
		/prevention of endometriosis and related conditions.
		Additional highly preferred indications include fibromas,
		heart disease, cardiac arrest, heart valve disease, and

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					disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) Additional preferred indications include inflammation and inflammation and observed disorders (e.g., as described below).
	0978 1211	9		TOTAL DEFENDANCE VOLUME	inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
166	HFEAY59	089	Production of IFN gamma using a T	IFNgamma FMAT. IFNg plays a central role in the immune system and is	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory cytokine. IFNg promotes TH1 and	An alternative highly preferred embodiment of the invention includes a method for inhibiting the production
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				MHC expression. Assays for	Activity, Dioda-Related Disorders, analyoi "Cardiovascular Disorders"), and infection (e.g., viral
	·			immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
				helper cell functions are well known in the	Highly preferred indications include autoimmune disease
				to assess the ability of polypeptides of the	(e.g., incumatoria arminis, systemic tupus erymematosis, multiple sclerosis and/or as described below),
				invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
				agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
				mediate immunomodulation, regulate inflammatory activities modulate TH2	mediated immune response. Additional highly preferred indications include inflammation and inflammatory.
	-			helper cell function, and/or mediate	disorders. Additional preferred indications include
				humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
				Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
				immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
				production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
				gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
				cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
				routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,

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Cuner preterred indicates disorders and prefor example, hyperplas Preferred indications leukopenia, disease, acute lymphoc, multiple myeloma, AIDS, granulomatous isease, sepsis, neutropession of immune reactifis, hemophilia, littus, endocarditis, ima and allergy.	nclude usir les, agonist is, preventi ar Disease,
: Other pre e disorders for examp Preferrect also disease, ac disease, ac s, multiple AIDS, gran lisease, sep ssion of im s, hemoph hma and all hma an	invention i or antibodi on, diagnos ion, Vascul and Stroke
nary cancer proliferativ ns, such as dysplasia. ncytopenia Hodgkin's smacytoma a, arthritis, ory bowel c isis, suppre isis, suppre isi, suppre	ents of the invention () in detection Inflammat estenosis, a
brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
	Preferre polypep antagon and/or ti Athereo
cluding onists of disclosed redisclosed what a salez et al., 995); 856:22-32 Immunol ttology he contents prorated an T cells ese assays significant un un un un un un un veness to veness to	tr and ad to of the of the of the ention) to templary telly pression tos P, et al, and,
vention (ir vention) (ir vention) (ir vention) (ir vention) (ir vention); Romolecula (1999); Romolo); Gonz (225-233 (125-233 (125-233 (126-233)); Annu Rev (1999); Annu Rev (1999); Therein inconirety. Humording to the control of the	expression wn in the a who in the a lely modifie olypeptides olypeptides a sof the inversion. Exercision. Exercisi
immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1998); Boehm et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol.
immunom polypeptic antibodies the invent in Miragli Screening al., "Lymp Chapter 6 J Clin Lab Billiau et a (1998); Be (15:749-79 (Oxford) 3 of each of by referen that may be isc herein or c Human T lymphocyt express a or CD8. T cell-media preactivate immunom	Assays for ICAM-1 a may be use assess the invention (agonists or regulate IC assays that modified to include ass FASEB J, Miyamoto
	ICAM-1
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				al., Iransp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell	as, leukema, lympnoma, prostate, oreast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
168	HFIHZ75	682	Production of TNF alpha by T cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate inflammation and cytotoxicity, and mediate humoral and/or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as leukemia lymphoma melanoma officinal dispanse and cancers, such

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169 HFIJA29 683 Product	Production of IL-4	antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 16(199); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells. T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immune and immunomodulation, stimulate immune	malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectiou (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of the invention includes asthma. A highly preferred indication includes allergy. A highly preferred indication includes allergy. A highly preferred indication includes rhinits. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include inflammation includes method for the invention includes reactions include inflammation and inflammatory disorders.
		cens, inoquiate initionic cen potatization, and/or mediate humoral or cell-mediated	metanoma, and/or as described below under "Hynemroliferative Disorders") Preferred indications

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				minimum, Exclimptally assays that test 101	iliciuuc licopiasilis aliu caliceis, sucii as, loi exallipie,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and prostate, breast,
				production of cytokines, such as IL-4, and	lung, colon, pancreatic, esophageal, stomach, brain, liver
				the stimulation of immune cells, such as B	and urinary cancer. Other preferred indications include
				cells, T cells, macrophages and mast cells.	benign dysproliferative disorders and pre-neoplastic
			-	Such assays that may be used or routinely	conditions, such as, for example, hyperplasia, metaplasia,
				modified to test immunomodulatory	and/or dysplasia. Preferred indications include blood
				activity of polypeptides of the invention	disorders (e.g., as described below under "Immune
				(including antibodies and agonists or	Activity", "Blood-Related Disorders", and/or
				antagonists of the invention) include the	"Cardiovascular Disorders"). Preferred indications include
				assays disclosed in Miraglia et al., J	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				Biomolecular Screening 4:193-204 (1999);	lupus erythematosis, multiple sclerosis and/or as described
				Rowland et al., "Lymphocytes: a practical	below) and immunodeficiencies (e.g., as described below).
				approach" Chapter 6:138-160 (2000);	Preferred indications include anemia, pancytopenia,
				Gonzalez et al., J Clin Lab Anal 8(5):277-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				283 (1194); Yssel et al., Res Immunol	lymphocytic anemia (ALL), plasmacytomas, multiple
				144(8):610-616 (1993); Bagley et al., Nat	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				Immunol 1(3):257-261 (2000); and van der	granulomatous disease, inflammatory bowel disease,
				Graaff et al., Rheumatology (Oxford)	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				38(3):214-220 (1999), the contents of each	immune reactions to transplanted organs and tissues,
				of which are herein incorporated by	hemophilia, hypercoagulation, diabetes mellitus,
				reference in its entirety. Human T cells	endocarditis, meningitis, and Lyme Disease. An
				that may be used according to these assays	additonal preferred indication is infection (e.g., an
				may be isolated using techniques disclosed	infectious disease as described below under "Infectious
				herein or otherwise known in the art.	Disease").
				Human T cells are primary human	
				lymphocytes that mature in the thymus and	
		•		express a T cell receptor and CD3, CD4, or	
-				CD8. These cells mediate humoral or cell-	
				mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
169	HFIJA29	683		CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention
			and activation of T cells	expression is restricted to activated T cells.	includes a method for activating T cells. An alternative
				CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
					or i
				has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the

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	autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
	CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
	immunoresponses. Assays for	of the invention includes a method for stimulating T cell
	immunomodulatory proteins important in	proliferation. Highly preferred indications include
	the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
	expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
	CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications
	may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
•	assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
	invention (including antibodies and	described below), immunodeficiencies (e.g., as described
	agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
	modulate the activation of T cells,	suppressing a T cell-mediated immune response.
	maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
	mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
	immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
	immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
	upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
	as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
	Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
	modified to test immunomodulatory	Other preferred indications include benign dysproliferative
-	activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
	(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
	antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
	example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
	et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
	(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
	practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
	(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
	77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
	Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
	Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
	321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
	are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
	entirety. Human T cells that may be used	described below under "Infectious Disease").
	according to these assays may be isolated	
	using techniques disclosed herein or	
	otherwise known in the art. Human T cells	

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ell e	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer. ch M., M., es es es es es es es es es e	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation. Vascular Disease.
are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, differentiation., and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345 (2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakamoto H, et al., J Biol Chem, 275(46):35857-35862 (2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the mouse CTLL cell line.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the
	Proliferation, differentiation, and/or cytokine production in immune cells (such as T-cells).	Production of ICAM-1
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				invention (including antibodies and	Athereosclerosis, Restenosis, and Stroke
				agonists or antagonists of the invention) to	
				regulate ICAIN-1 expression. Exemplary	
				assays that may be used or routinely	
				modified to measure ICAM-1 expression	
			1	include assays disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281 (2001); and,	
				Miyamoto K, et al., Am J Pathol,	
				156(5):1733-1739 (2000), the contents of	
				each of which is herein incorporated by	
				reference in its entirety. Cells that may be	
				used according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				cells that may be used according to these	
				assays include microvascular endothelial	
				cells (MVEC).	
172 HFKEU12	3U12	989	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
	•		serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
*			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
	•			invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
		-		Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,

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			Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitr's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
173	HFPCZ55	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the	A highly preferred indication is diabetes mellitus. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment

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				invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious
				EN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 130(4):1404 of 1608); Ellist ED, 24 al.	tion t
				1.57(4).14574-7 (1550), rugi 5R, et al., J Biol Chem 1998 Jul 10;273(28):17771-9	contracture). An additional mgniy preferred indication is obesity and/or complications associated with
				(1998), the contents of each of which is	cations
				herein incorporated by reference in its entirety. Pancreatic cells that may be used	weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated
				according to these assays are publicly	with insulin resistance.
				available (e.g., through the ATCC) and/or	
				may be rounnerly generated. Exemplary pancreatic cells that may be used	
		-		according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
-				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
174	HFPDR62	889	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including announces and	anticremant of the invention includes a mathod for
				agonists of anidagonists of the invention of promote or inhibit cell proliferation	inhibiting adjuvented differentiation
				activation and differentiation Exemplary	numbring authors to universition. A inguistred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adinocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly

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 agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
al Biol Chem 379(8-9):1101-1110	described below under Endocrine Disorders). Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
 410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
 be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
 •	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.

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175 HFPDS07	Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benigm dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or such as, for example, hyperplasia, metaplasia, and/or	Activation of Natural Kinase assay. Kinase assay, for example Killer Cell ERK an Elk-1 kinase assay, for ERK signal Signaling Pathway. Killer Cell ERK an Elk-1 kinase assay, for ERK signal Signaling Pathway. An include a method for simulating natural killer cell proliferation includes a method for invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation. Activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) includes a method for inhibiting natural killer cell ambodiment of the invention includes a method for inhibiting natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of described below under "Immune Activity", and/or "Blood-Related agonists or antagonists of the invention includes and under "Immune Activity", Preferred infortation (including antibodies and agonists or antagonists of the invention) to propagate activity that may be under "Immune Activity", Preferred infortation and unde
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				(1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have cytolytic and cytotoxic activity) or primary NK cells.	indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include benign dysproliferative brain, liver, urinary cancer, lymphoma and leukemias. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and
175	HFPDS07	689	Upregulation of HLA-DR and activation of T cells	HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+ T cells. Deregulation of MHC class II has been associated with autoimmune diseases (e.g., diabetes, rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis). Assays for immunomodulatory proteins expressed on MHC class II expressing T cells and antigen presenting cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and alternatively, suppressing a T cell-mediated immune response. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section

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humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
 upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as
polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
 assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
 Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
Gansbacher and Zier, Cell Immunol	complications associated with obesity. Additional highly
117(1):22-34 (1988); and Itoh et al., J	preferred indications include weight loss or alternatively,
 Histochem Cytochem 40(11):1675-1683,	weight gain. Aditional highly preferred indications
the contents of each of which are herein	are complications associated with insulin resistance.
incorporated by reference in its entirety.	Additional highly preferred indications are disorders of the
Human T cells that may be used according	musculoskeletal systems including myopathies, muscular
to these assays may be isolated using	dystrophy, and/or as described herein.
techniques disclosed herein or otherwise	additional preferred indication is infection (e.g., AIDS,
known in the art. Human T cells are	and/or as described below under "Infectious Disease").
primary human lymphocytes that mature in	Preferred indications include endocrine disorders (e.g., as
the thymus and express a T Cell receptor	described below under "Endocrine Disorders"), and
and CD3, CD4, or CD8. These cells	neoplastic diseases (e.g., leukemia, lymphoma, and/or as
mediate humoral or cell-mediated	described below under "Hyperproliferative Disorders").
immunity and may be preactivated to	Preferred indications include neoplasms and cancer, such
enhance responsiveness to	as, for example, leukemia, lymphoma, and prostate, breast,
immunomodulatory factors.	lung, colon, pancreatic, esophageal, stomach, brain, liver
	and urinary cancer. Other preferred indications include
	benign dysproliferative disorders and pre-neoplastic
	conditions, such as, for example, hyperplasia, metaplasia,

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				and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and
176 HFRAB10	069	Production of MIP1alpha	MIP-lalpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention
			chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune").
			agonists of antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as	"Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications
			(MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antihodies and	Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sensis neutronenia neutronhilia neoriasis sunnession of
			agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll	immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly

		-		Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., 1 ransp 1mmunol 8(1):1/-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
177	HFTBM38	1691	Upregulation of CD152	CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention
			and activation of T cells	expression is restricted to activated T cells.	includes a method for activating T cells. An alternative
				CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				proliferation. Reduced CD152 expression	method for inhibiting the activation of and/or inactivating
				has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
				autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
				CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
				immunoresponses. Assays for	of the invention includes a method for stimulating T cell
				immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
				expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
				CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications
				may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
				assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
				invention (including antibodies and	described below), immunodeficiencies (e.g., as described
				agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
				modulate the activation of T cells,	suppressing a T cell-mediated immune response.
				maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
				immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,

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				as CD152, and the activation of 1 cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
	*			antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
177	HFTBM38	691	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple

				Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	ceg., as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, thrombocytopenia, Hodgkin's disease, neutropenia, hypercoagulation, diabetes mellitus, endocarditis, meutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
178	HFTDH56	692	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred

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apoptosis. Induction of apoptosis in	metho	
endothelial cells supporting the vasculature	inhibiting endothelial cell proliferation. A highly	
of tumors is associated with tumor	preferred embodiment of the invention includes a method	
regression due to loss of tumor blood	for stimulating apoptosis of endothelial cells. An	
supply. Exemplary assays for caspase	alternative highly preferred embodiment of the invention	
apoptosis that may be used or routinely	includes a method for inhibiting (e.g., decreasing)	
 modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred	
of polypeptides of the invention (including	embodiment of the invention includes a method for	
antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred	
the invention) include the assays disclosed	embodiment of the invention includes a method for	
in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred	
(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for	
218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly	
Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method	
the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred	
incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described	
 Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and	
according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,	
available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,	
sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular	
may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular	
include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac	
(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic	
endothelial cells which line blood vessels	overload, and/or as described below under	
and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications	
but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic	
vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such	
immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels	
	themselves, such as of the arteries, capillaries, veins and/or	
	lymphatics). Highly preferred are indications that	
	stimulate angiogenesis and/or cardiovascularization.	
	Highly preferred are indications that inhibit angiogenesis	
	and/or cardiovascularization. Highly preferred	
	indications include antiangiogenic activity to treat solid	
	tumors, leukemias, and Kaposi's sarcoma, and retinal	
	disorders. Highly preferred indications include neoplasms	
	and cancer, such as, Kaposi's sarcoma, hemangioma	

(capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's disease and Reynaud's phenomenom, aneurysms, restenosis; venous and lymphatic disorders	such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection,	disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below).

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					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
					and Crohn's disease), and pain management.
179	HFVGK35	693	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute

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				a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell approach the content of the	lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
H 6/1	HFVGK35	693	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assays that may be used or routinely modified to test immunomodulatory and diffierentiation activity of polypeptides of the invention (including antibodies and agonists or	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs

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				assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation	mellitus, endocarditis, meningitis (bacterial and viral), Lyme Disease, asthma, and allergy Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
<u> </u>	HFVHW43	440	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below)
				antibodies and agonists or antagonists of the invention) include assays disclosed in:	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious

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HFXAV37	\$ \$69	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway	Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167. Kinase assay. Kinase assays, for Pt3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for Pt3 kinase activity that may be used or routinely modified to test Pt3 kinase-induced activity of	diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. A highly preferred embodiment of the invention includes a method for increasing muscle cell survival. A preferred embodiment of the invention includes a method for decreasing muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred for inhibiting muscle cell proliferation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell proliferation is lubilited. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation is inhibited. A preferred embodiment of the invention includes a method for stimulating muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation. In a specific embodiment, skeletal
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the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is
1110 (1998); Nikoulina et al., Diabetes	inhibited. Highly preferred indications include disorders
49(2):263-271 (2000); and Schreyer et al.,	of the musculoskeletal system. Preferred indications
 contents of each of which are herein	"Hyperproliferative Disorders", endocrine disorders (e.g.,
incorporated by reference in its entirety.	as described below under "Endocrine Disorders"), neural
Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
available (e.g., through the ATCC).	described below under "Immune Activity",
Exemplary rat myoblast cells that may be used according to these assays include I 6	"Cardiovascular Disorders", and/or "Blood-Related Disorders") immine disorders (e.g., as described below)
cells. I f is an adherent rat mychlast cell	under "Immine Activity") and infection (e.g., as
line, isolated from primary cultures of rat	described below under "Infectious Disease").
thigh muscle, that fuses to form	s,
multinucleated myotubes and striated	additional highly preferred indication is a complication
fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
	diabetic nephropathy, kidney disease (e.g., renal failure,
	nephropathy and/or other diseases and disorders as
	described in the "Renal Disorders" section below), diabetic
	neuropathy, nerve disease and nerve damage (e.g, due to
	diabetic neuropathy), blood vessel blockage, heart disease,
	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infections (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below, especially of the urinary tract and
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					is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal system including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.
182	HFXBN86	969	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple

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				modified to test immunomodulatory and	myeloma. Burkitt's lymphoma, arthritis. AIDS.
				chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
				invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
		•		agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
				include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
				J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
				a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
				Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
•				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
183	HFXBT66	269	Production of IL-2 and	IL-2 FMAT. IL-2 is the principal T cell	A highly preferred embodiment of the invention
			activation of T cells	factor that allows T cell expansion and	includes a method for stimulating IL-2 production. An
				differentiation into effector cells. Assays	alternative highly preferred embodiment of the invention
				for immunomodulatory proteins secreted	includes a method for inhibiting (e.g., reducing) IL-2
				by TH1 cells that promote T cell and NK	production. A highly preferred embodiment of the
				cell growth and differentiation are well	invention includes a method for stimulating T cell
				known in the art and may be used or	expansion. An alternative highly preferred embodiment of
				routinely modified to assess the ability of	the invention includes a method for inhibiting T cell
				polypeptides of the invention (including	expansion. A highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for stimulating T cell
				the invention) to mediate	differentiation. In a specific embodiment, this method
				immunomodulation, promote immune cell	stimulates T cell differentiation into effector cells. An
				growth and differentiation, and/or mediate	alternative highly preferred embodiment of the invention

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	humoral or cell-mediated immunity.	includes a method for inhibiting T cell differentiation. In a
	Exemplary assays that test for	specific embodiment, this method inhibits the
	immunomodulatory proteins evaluate the	differentiation of T cells into effector cells. Highly
	production of cytokines, such as IL-2, and	preferred indications include neoplastic diseases (e.g.,
	the activation of T cells. Such assays that	melanoma, renal cell carcinoma, leukemia, lymphoma,
	may be used or routinely modified to test	and/or as described below under "Hyperproliferative
	immunomodulatory activity of	Disorders"). Highly preferred indications include
	polypeptides of the invention (including	neoplasms, such as, for example, melanoma (e.g.,
	antibodies and agonists or antagonists of	metastatic melanoma), renal cell carcinoma (e.g.,
	the invention) include the assays disclosed	metastatic renal cell carcinoma), leukemia, lymphoma
	in Miraglia et al., J Biomolecular	(e.g., T cell lymphoma), and prostate, breast, lung, colon,
	Screening 4:193-204 (1999); Rowland et	pancreatic, esophageal, stomach, brain, liver, ovarian, and
	al., "Lymphocytes: a practical approach"	urinary cancer. Other preferred indications include benign
	Chapter 6:138-160 (2000); Laduda et al.,	dysproliferative disorders and pre-neoplastic conditions,
	Immunology 94(4):496-502 (1998); and	such as, for example, hyperplasia, metaplasia, and/or
	Powell et al., Immunol Rev 165:287-300	dysplasia. A highly preferred indication is infection (e.g.,
	(1998), the contents of each of which are	an infectious disease as described below under "Infectious
	herein incorporated by reference in its	Disease"). A highly preferred indication is AIDS and HIV
	entirety. Human T cells that may be used	infection. Additional highly preferred indications include
	according to these assays may be isolated	suppression of immune reactions to transplanted organs
	using techniques disclosed herein or	and/or tissues, uveitis, psoriasis, and tropical spastic
	otherwise known in the art. Human T cells	paraparesis. Preferred indications include blood
	are primary human lymphocytes that	disorders (e.g., as described below under "Immune
	mature in the thymus and express a T cell	Activity", "Blood-Related Disorders", and/or
	receptor and CD3, CD4, or CD8. These	"Cardiovascular Disorders"). Preferred indications include
-	cells mediate humoral or cell-mediated	autoimmune diseases (e.g., rheumatoid arthritis, systemic
	immunity and may be preactivated to	lupus erythematosis, multiple sclerosis and/or as described
	enhance responsiveness to	below), immunodeficiencies (e.g., as described below),
	immunomodulatory factors.	organ and tissue transplant rejection. Additional
		preferred indications include inflammation and
		inflammatory disorders. Preferred indications include
		anemia, pancytopenia, leukopenia, thrombocytopenia,
		Hodgkin's disease, acute lymphocytic anemia (ALL),
		plasmacytomas, multiple myeloma, Burkitt's lymphoma,
		Non-Hodgkin's lymphoma, Kaposi's sarcoma arthritis,
		granulomatous disease, inflammatory bowel disease,
		Hepatitis (e.g. Hepatitis C), sepsis, neutropenia,

					neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
184	HFXFZ46	869	Upregulation of HLA-DR and activation of T cells	HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+ T cells. Deregulation of MHC class II has	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular
				been associated with autoimmune diseases	Disorders"). Highly preferred indications include
				systemic lupus erythematosis, and multiple	autominimus diseases (e.g., intentiatora artificia), systemic lupus erythematosis, multiple sclerosis and/or as described
		·· · · · · · · · · · · · · · · · · · ·		sclerosis). Assays for immunomodulatory proteins expressed on MHC class II	below) and immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and
				expressing T cells and antigen presenting	alternatively, suppressing a T cell-mediated immune
				cells are well known in the art and may be used or routinely modified to assess the	response. A highly preferred indication is diabetes mellitus. An additional highly preferred indication
				ability of polypeptides of the invention	is a complication associated with diabetes (e.g., diabetic
				(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
				antagonists of the invention) to modulate the activation of T cells, and/or mediate	renal failure, nephropathy and/or other diseases and
				humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
				Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
				immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
				upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
				such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
				activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
				be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
				minimitation activity of polymentides of the invention (including	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section
				antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
				the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
				assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
				Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
				Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
				approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
				Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
				89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
				Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
				Gailsoacher and zier, Ceil Immunol	complications associated with obesity. Additional highly

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				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
			-	activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
		··, ,		assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
	•			Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety.	anemia (ALL), plasmacytomas, multiple myeloma,
				Mouse T cells that may be used according	Burkitt's lymphoma, granulomatous disease, inflammatory
				to these assays are publicly available (e.g.,	bowel disease, sepsis, psoriasis, suppression of immune
				through the ATCC). Exemplary mouse T	reactions to transplanted organs and tissues, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease.
				assays include the HT2 cell line, which is	
-				an IL-2 dependent suspension culture cell	
				line that also responds to IL-4.	
185	HGBER72	669	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			NFAT response in	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
			immune cells (such as	known in the art and may be used or	Disorders"). Highly preferred indications include
			T-cells).	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
				antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),
				the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
				transcription factors and modulate	suppressing a T cell-mediated immune response.
				expression of genes involved in	Additional highly preferred indications include
				immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
				assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
				response element that may be used or	disease as described below under "Infectious Disease").
				routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,

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				civilizing activity of polypopulaes of the	icancilla, lyllipilollia, allacol as acselloca below ullaci
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.
				ATCC). Exemplary human T cells that	
				may be used according to these assays	
				include the JURKAT cell line, which is a	
				suspension culture of leukemia cells that	
				produce IL-2 when stimulated.	
185	HGBER72	669	Activation of	Assays for the activation of transcription	Highly preferred indications include inflammation and
			transcription through	through the NFKB response element are	inflammatory disorders. Highly preferred indications
			NFKB response	well-known in the art and may be used or	include blood disorders (e.g., as described below under
			element in immune	routinely modified to assess the ability of	"Immune Activity", "Blood-Related Disorders", and/or
			cells (such as T-cells).	polypeptides of the invention (including	"Cardiovascular Disorders"). Highly preferred indications
				antibodies and agonists or antagonists of	include autoimmune diseases (e.g., rheumatoid arthritis,
				the invention) to regulate NFKB	systemic lupus erythematosis, multiple sclerosis and/or as
				transcription factors and modulate	described below), and immunodeficiencies (e.g., as
				expression of immunomodulatory genes.	described below). An additional highly preferred
				Exemplary assays for transcription through	indication is infection (e.g., AIDS, and/or an infectious
				the NFKB response element that may be	disease as described below under "Infectious Disease").
				used or rountinely modified to test NFKB-	Highly preferred indications include neoplastic diseases
				response element activity of polypeptides	(e.g., melanoma, leukemia, lymphoma, and/or as described
				of the invention (including antibodies and	below under "Hyperproliferative Disorders"). Highly

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preferred indications include neoplasms and cancers, such as, for example, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly
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agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of
	Production of TNF alpha by dendritic cells
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preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-5 production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-5 production. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) immunoglobulin production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) immunoglobulin production. A highly preferred indication includes altergy. A highly preferred indication includes rhinitis. An additional highly preferred indication is infection (e.g., an infections
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	IL-5 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells, mast cells, basophils, and eosinophils that stimulate eosinophil function and B cell Ig production and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cell function, modulate B cell Ig production, modulate immune cell
	Production of IL-5
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				nolarization and/or mediate humoral or	disease as described below under "Infactions Disease")
				Coll modicing immediate.	arsonas as acsertiona octon aniaci anicomons Discuss),
				cen-mediated immunity. Exemplary	and initamination and initaminatory disorders.
				assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
				proteins evaluate the production of	described below under "Immune Activity", "Blood-
				cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
				stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
				cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
				be used or routinely modified to test	multiple sclerosis and/or as described below) and
				immunomodulatory activity of	immunodeficiencies (e.g., as described below).
				polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
				the invention) include the assays disclosed	below under "Hyperproliferative Disorders"). Preferred
				in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
				Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
				al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include
				Blood 92(9):3338-3345 (1998); Jung et al.,	benign dysproliferative disorders and pre-neoplastic
				Eur J Immunol 25(8):2413-2416 (1995);	conditions, such as, for example, hyperplasia, metaplasia,
				Mori et al., J Allergy Clin Immunol 106(1	and/or dysplasia. Preferred indications include anemia,
				Pt 2):558-564 (2000); and Koning et al.,	pancytopenia, leukopenia, thrombocytopenia, leukemias,
				Cytokine 9(6):427-436 (1997), the	Hodgkin's disease, acute lymphocytic anemia (ALL),
				contents of each of which are herein	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				incorporated by reference in its entirety.	arthritis, AIDS, granulomatous disease, inflammatory
				Human T cells that may be used according	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				to these assays may be isolated using	immune reactions to transplanted organs and tissues,
				techniques disclosed herein or otherwise	hemophilia, hypercoagulation, diabetes mellitus,
				known in the art. Human T cells are	endocarditis, meningitis, and Lyme Disease.
				primary human lymphocytes that mature in	
				the thymus and express a T cell receptor	
				and CD3, CD4, or CD8. These cells	
				mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
		,		immunomodulatory factors.	
188	HGBHP91	702	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription via	through the DMEF1 response element are	An additional highly preferred indication is a complication
			DMEF1 response	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,

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diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or			
routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4	promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive of transporter in	fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Thai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA	binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly
element in adipocytes and pre-adipocytes			

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				available (e.g., through the ATCC) and/or may be routinely generated. Exemplary	
				cells that may be used according to these	
				assays include the mouse 3T3-L1 cell line	
				which is an adherent mouse preadipocyte	
				cell line. Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3 fibroblasts	
				developed through clonal isolation. These	
				cells undergo a pre-adipocyte to adipose-	
				like conversion under appropriate	
				differentiation culture conditions.	
189	HGCAC19	703	Activation of	Assays for the activation of transcription	A highly preferred embodiment of the invention
			transcription through	through the CD28 response element are	includes a method for stimulating T cell proliferation. An
			CD28 response element	well-known in the art and may be used or	alternative highly preferred embodiment of the invention
			in immune cells (such	routinely modified to assess the ability of	includes a method for inhibiting T cell proliferation. A
			as T-cells).	polypeptides of the invention (including	highly preferred embodiment of the invention includes a
				antibodies and agonists or antagonists of	method for activating T cells. An alternative highly
				the invention) to stimulate IL-2 expression	preferred embodiment of the invention includes a method
				in T cells. Exemplary assays for	for inhibiting the activation of and/or inactivating T cells.
				transcription through the CD28 response	A highly preferred embodiment of the invention includes a
				element that may be used or routinely	method for stimulating (e.g., increasing) IL-2 production.
				modified to test CD28-response element	An alternative highly preferred embodiment of the
				activity of polypeptides of the invention	invention includes a method for inhibiting (e.g., reducing)
				(including antibodies and agonists or	IL-2 production. Additional highly preferred
				antagonists of the invention) include	indications include inflammation and inflammatory
				assays disclosed in Berger et al., Gene	disorders. Highly preferred indications include
				66:1-10 (1998); Cullen and Malm,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
				Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
				85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
				Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. An
				(1997); Parra et al., J Immunol	additional highly preferred indication includes infection
				166(4):2437-2443 (2001); and Butscher et	(e.g., AIDS, and/or as described below under "Infectious
				al., J Biol Chem 3(1):552-560 (1998), the	Disease"). Highly preferred indications include
				contents of each of which are herein	neoplastic diseases (e.g., melanoma, renal cell carcinoma,
				incorporated by reference in its entirety. T	leukemia, lymphoma, and/or as described below under
				cells that may be used according to these	"Hyperproliferative Disorders"). Highly preferred

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	·		assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal carcinoma (e.g., metastatic renal cell carcinoma), leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is infection (e.g., tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). A highly preferred indication is ATDC Additional highly preferred
				indications in ALDs. Additional inginy preferror indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes and allergy.
190 HGCAC19 7	704	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a

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Methods in En Henthorn et al. 85:6342-6346 Iacobelli, J Im (1997); Parra e 166(4):2437-2 al., J Biol Cher contents of eac incorporated by cells that may l assays are publ the ATCC). E; may be used ac include the JUI suspension culf produce IL-2 w	element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include inflammatory disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. An additional highly preferred indication includes infections Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under "Thyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma (e.g., metastatic renal cell carcinoma), elukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is AIDS. Additional highly preferred indication is alove an infectious disease as described below under "Infectious Disease"). A highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and/or include Superessis, and described below under gegons and/or tissues, uveitis, psoriasis, and/or dysladers (e.g., as described below under belowing." "Hyperplases").	
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				include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
191 HGCAC19	705	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety.	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include autoimmune diseases (e.g., theumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. An additional highly preferred indication includes infection (e.g., AIDS, and/or as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under
			cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays	"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma (e.g., metastatic renal cell carcinoma),

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indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic neuropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or stroke, impotence (e.g., due to diabetic neuropathy or stroke, impotence (e.g., due to diabetic neuropathy or stroke, impotence (e.g., due to diabetic neuropathy or	on of insul I may be u ss the abili ion (incluc itagonists c sulin lin secretic anti-rat anti-rat scretion fre	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from paragraphs of the invention by the follogic integral from the insulin antibodies.	Insulin Secretion Assays for measuring secreticate well-known in the art and or routinely modified to asset of polypeptides of the invention antibodies and agonists or art the invention) to stimulate in secretion. For example, insulin secretion antibodies. Insulin secretion and agonists or art the invention is measured by FMAT using insulin antibodies. Insulin secretion and agonic		Insulin Secretion
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				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension.
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
				(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
				Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
				Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
,				865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
				Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
				Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
				Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
				of each of which is herein incorporated by	with insulin resistance.
				reference in its entirety. Pancreatic cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC) and/or may be routinely generated.	
				Exemplary pancreatic cells that may be	
				used according to these assays include	
				HITT15 Cells. HITT15 are an adherent	
				epithelial cell line established from Syrian	
				hamster islet cells transformed with SV40.	
		·		These cells express glucagon,	
				somatostatin, and glucocorticoid receptors.	
				The cells secrete insulin, which is	
				stimulated by glucose and glucagon and	
				suppressed by somatostatin or	
				glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
193	HHEGS55	707	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the

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	ability of nolymentides of the invention	invention metaces a metalog 101 summating (c.g., increasing) TME alaba anaduction. Deferred indications
 45 1-50115):	(including antibodies and agonists or	include blood disorders (e.g., as described below under
	antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
	the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
	the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
	growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
	transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
	used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
	activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
	invention (including antibodies and	immune response. Additional highly preferred indications
	agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
 	include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
	Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
	Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
	Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
	85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
	Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
	content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
	incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
	cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
	assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
	the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
	may be used according to these assays	pre-neoplastic conditions, such as, for example,
	include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
	2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
	with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
		anemia (ALL), plasmacytomas, multiple myeloma,
		Burkitt's lymphoma, arthritis, AIDS, granulomatous
		disease, inflammatory bowel disease, neutropenia,
		neutrophilia, psoriasis, suppression of immune reactions to
		transplanted organs and tissues, hemophilia,
		hypercoagulation, diabetes mellitus, endocarditis,
		asthma and allergy. An additional preferred indication
		is infection (e.g., an infectious disease as described below
		under "Infectious Disease").

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r A highly preferred embodiment of the invention oduced by includes a method for stimulating MPI a production. An	`	ell includes a method for inhibiting (e.g., reducing) MIP1a		ied to (e.g., an infectious disease as described below under	es of the "Infectious Disease"). Preferred indications include			-							Such								mphocytes: allergy. Preferred indications also include neoplastic	:138-160 diseases (e.g., leukemia, lymphoma, and/or as described		Orakes et preferred indications include neoplasms and cancers, such	(2000); as, leukemia, lymphoma, prostate, breast, lung, colon,		, J Leukoc cancer. Other preferred indications include benign	ntents of dysproliferative disorders and pre-neoplastic conditions,				hniques	
MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by	activated dendritic cells that upregulate	monocyte/macrophage and T cell	chemotaxis are well known in the art and	may be used or routinely modified to	assess the ability of polypeptides of the	invention (including antibodies and	agonists or antagonists of the invention) to	mediate immunomodulation, modulate	chemotaxis, and modulate T cell	differentiation. Exemplary assays that test	for immunomodulatory proteins evaluate	the production of chemokines, such as	macrophage inflammatory protein 1 alpha	(MIP-1a), and the activation of	monocytes/macrophages and T cells.	assays that may be used or routinely	modified to test immunomodulatory and	chemotaxis activity of polypeptides of the	invention (including antibodies and	agonists or antagonists of the invention)	include assays disclosed in Miraglia et al.,	J Biomolecular Screening 4:193-	204(1999); Rowland et al., "Lymphocytes:	a practical approach" Chapter 6:138-160	(2000); Satthaporn and Eremin, J R Coll	Surg Ednb 45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-29 (2000);	Verhasselt et al., J Immunol 158:2919-	2925 (1997); and Nardelli et al., J Leukoc	Biol 65:822-828 (1999), the contents of	each of which are herein incorporated by	reference in its entirety. Human dendritic	cells that may be used according to these	assays may be isolated using techniques	
Production of MIP1alpha	: :																				-														
708									-																										
HHEOW19																																			
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				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
			-	cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
194	HHEOW19	208	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-
				routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
				polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
				antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
				immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
				inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
				assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
				alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
				inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
				response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
				routinely modified to test	leukemia, lymphoma, and/or as described below under
				immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
				polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
				antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
				Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
				4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
				"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
				Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
				al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
				(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,

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				Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are	granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of
				herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
				entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
				be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
				isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
				or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
				dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
				in suspension culture, which, when	Disease").
			****	activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation and functional activities.	
194	HHEOW19	708	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
		•		are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
				(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
				Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
				Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
					indication is obesity and/or complications associated with
				Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include

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weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional
Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells, B cells, and most proliferating cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunity.
	Upregulation of CD71 and activation of T cells
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				initiational action of the following chains and the first the firs	inging preferred informations include infection.
				uplegulation of cell surface markers, such	indications include neopiastic diseases (e.g., leukemia,
				as CD/1, and the activation of 1 cells.	lymphoma, and/or as described below under
				Such assays that may be used or routinely	"Hyperproliferative Disorders"). Preferred indications
-				modified to test immunomodulatory	include neoplasms and cancers, such as, for example,
				activity of polypeptides of the invention	leukemia, lymphoma, melanoma, and prostate, breast,
				(including antibodies and agonists or	lung, colon, pancreatic, esophageal, stomach, brain, liver
				antagonists of the invention) include, for	and urinary cancer. Other preferred indications include
				example, the assays disclosed in Miraglia	benign dysproliferative disorders and pre-neoplastic
				et al., J Biomolecular Screening 4:193-204	conditions, such as, for example, hyperplasia, metaplasia,
				(1999); Rowland et al., "Lymphocytes: a	and/or dysplasia. Preferred indications include anemia,
				practical approach" Chapter 6:138-160	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				(2000); and Afetra et al., Ann Rheum Dis	disease, acute lymphocytic anemia (ALL), plasmacytomas,
-				52(6):457-460 (1993), the contents of each	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
				reference in its entirety. Human T cells	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				that may be used according to these assays	immune reactions to transplanted organs and tissues,
				may be isolated using techniques disclosed	hemophilia, hypercoagulation, diabetes mellitus,
				herein or otherwise known in the art.	endocarditis, meningitis, Lyme Disease, and asthma and
				Human T cells are primary human	allergy.
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
\dashv				immunomodulatory factors.	
196 HHFFL34	T_34	710	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SKE that may be	sclerosis and/or as described below), immunodeficiencies

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			used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
			activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
			invention (including antibodies and	immune response. Additional highly preferred indications
			agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
			include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
			Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
			Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
			Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
			85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
			Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
			content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
			incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
			cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
			assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
			the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
			may be used according to these assays	pre-neoplastic conditions, such as, for example,
			include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
	-		2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
			with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				anemia (ALL), plasmacytomas, multiple myeloma,
				Burkitt's lymphoma, arthritis, AIDS, granulomatous
				disease, inflammatory bowel disease, neutropenia,
				neutrophilia, psoriasis, suppression of immune reactions to
				transplanted organs and tissues, hemophilia,
				hypercoagulation, diabetes mellitus, endocarditis,
-				meningitis, Lyme Disease, cardiac reperfusion injury, and
				asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious disease as described below
+				under "Infectious Disease").
19/ HHFFS40	11/	Endothelial Cell	Caspase Apoptosis. Assays for caspase	A highly preferred embodiment of the invention
		Apoptosis	apoptosis are well known in the art and	includes a method for stimulating endothelial cell growth.
-			may be used or routinely modified to	An alternative highly preferred embodiment of the
			assess the ability of polypeptides of the	invention includes a method for inhibiting endothelial cell
			invention (including antibodies and	growth. A highly preferred embodiment of the
			agonists or antagonists of the invention) to	invention includes a method for stimulating endothelial
			promote caspase protease-mediated	cell proliferation. An alternative highly preferred
			apoptosis. Induction of apoptosis in	embodiment of the invention includes a method for

endothelial cells supporting the vasculature	inhibiting endothelial cell proliferation. A highly
of tumors is associated with tumor	preferred embodiment of the invention includes a method
regression due to loss of tumor blood	for stimulating apoptosis of endothelial cells. An
supply. Exemplary assays for caspase	alternative highly preferred embodiment of the invention
apoptosis that may be used or routinely	includes a method for inhibiting (e.g., decreasing)
modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred
of polypeptides of the invention (including	embodiment of the invention includes a method for
antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred
the invention) include the assays disclosed	embodiment of the invention includes a method for
in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred
(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for
218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method
the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred
incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described
Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and
according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
 include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
endothelial cells which line blood vessels	overload, and/or as described below under
and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
	themselves, such as of the arteries, capillaries, veins and/or
	lymphatics). Highly preferred are indications that
	stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,

bucillary angiomatosis, hermangicendothelioma, angiosotrom, Highly preferred indications also include carters such as, prostate, breast, lung, colon, panceratic, esophageal, storneth, brain, liver, and uninary cancer. Preferred indications include benign depopulgative conditions, such as, for example, hyperplasia, metaplisate, and/or depoplasia, desage, inflammotory vascultides, such as include formers and by metaplications also include transparent and by metaplications and other vascular disease, and cancer. Highly preferred indications and treatment fraution, scarring, stehenia repertisation injuty, rehamatoid arthritis, creditovascular disease, such as peripheral vascular disease, and and seases such as a cause mental filture, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diductic or other ethological confidences are, and a diseases such as a cause mental filture, and osteoporosis, and congulative disorders, vascularitis, lymph angiogenesis, sevand disorders, such and secure and disorders, such and confidence in disease, and are set, heart value disease, and a series preferred indications include tolore bood disorders (e.g., as described below), and immunodes and menumental micrations include tolore, a described below), and immunodes and include trades cause and secure a

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					inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
197	HHFFS40	711	Production of TNF alpha by dendritic cells	INFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts.	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred
				smooth muscle, and other cell types that exert a wide variety of inflammatory and	embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are well known in the art and may be used or	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity". "Blood-
				routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
				polypeptides of the invention (including antibodies and agonists or antagonists of	Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
				the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
				immunomodulation, modulate inflammation and evtotoxicity. Exemplary	below), immunodeficiencies (e.g., as described below), hoosting a T cell-mediated immine response and
				assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
				alpha (TNFa), and the induction or	.si
				initiotition of an initialimatory of cytotoxic response. Such assays that may be used or	additional nightly preferred indication is sepsis. Highly preferred indications include neonlastic diseases (e.g.
				routinely modified to test	leukemia, lymphoma, and/or as described below under
				immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
				polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
				antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				the invention) include assays disclosed in Miraolia et al. I Biomolecular Screening	malignant glioma), solid tumors, and prostate, breast,
				4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
				"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
				Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
				al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
				(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., J Immunol 138:2919-2923 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				(1999) the contents of each of which are	granulomatous disease, inflammatory bowel disease,
				עה וויחווא זט וואס זט כווויווים אווי אווירון (עלכן)	neuropeina, neuropinia, psoriasis, suppression or

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				herein incompated by reference in its	immine reactions to transplanted organs and tissues
				entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
				be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
				isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
				or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
		·		dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
				in suspension culture, which, when	Disease").
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
197	HHFFS40	711	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is dispeted mallitue
		•	Flux in pancreatic heta	well brown in the out and may be used on	A additional bight anglement indication is unabeled inclinus.
			ın pancıcau	Well-Midwil III the all allu IIIay de used of	An additional inginy preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	skin), carpal tunnel syndrome and Dupuytren's
•				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated

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			entirety. Pancreatic cells that may be used	with insulin resistance
			according to these assays are publicly	
			according to diese assays are publicly	
			available (e.g., through the AICC) and/or	
			may be routinely generated. Exemplary	
			pancreatic cells that may be used	
			according to these assays include HITT15	
			Cells. HITT15 are an adherent epithelial	
			cell line established from Syrian hamster	
			islet cells transformed with SV40. These	
			cells express glucagon, somatostatin, and	
			glucocorticoid receptors. The cells secrete	
			insulin, which is stimulated by glucose and	
			glucagon and suppressed by somatostatin	
			or glucocorticoids. ATTC# CRL-1777	
			Refs: Lord and Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc. Natl. Acad.	
			Sci. USA 78: 4339-4343, 1981.	
198 HHGCS78	712	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
		transcription via	through the DMEF1 response element are	An additional highly preferred indication is a complication
		DMEF1 response	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
		element in adipocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
		and pre-adipocytes	polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
			antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
			the invention) to activate the DMEF1	neuropathy, nerve disease and nerve damage (e.g., due to
			response element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
			(such as that containing the GLUT4	stroke, impotence (e.g., due to diabetic neuropathy or
			promoter) and to regulate insulin	blood vessel blockage), seizures, mental confusion,
			production. The DMEF1 response	drowsiness, nonketotic hyperglycemic-hyperosmolar
			element is present in the GLUT4 promoter	coma, cardiovascular disease (e.g., heart disease,
			and binds to MEF2 transcription factor and	atherosclerosis, microvascular disease, hypertension,
			another transcription factor that is required	stroke, and other diseases and disorders as described in the
			for insulin regulation of Glut4 expression	"Cardiovascular Disorders" section below), dyslipidemia,
			in skeletal muscle. GLUT4 is the primary	endocrine disorders (as described in the "Endocrine
			insulin-responsive glucose transporter in	Disorders" section below), neuropathy, vision impairment
			fat and muscle tissue. Exemplary assays	(e.g., diabetic retinopathy and blindness), ulcers and
			that may be used or routinely modified to	impaired wound healing, and infection (e.g., infectious
			test for DMEF1 response element activity	diseases and disorders as described in the "Infectious

ng of d d d d d d d d d d d d d d d d d d					(in adipocytes and pre-adipocytes) by	Diseases" section below especially of the urinary tract and
antibodies and a genistis or antiagonists of infraction in contracture) the invention) include assays disclosed infraction in include assays disclosed infraction in include assays disclosed infraction in cat. J. Biol Chem. 269(45):28514. 21 (1592); Techne, 275(21):1632-8 (2000), Lin. highly preferred indications are complications assay to produce the invention of the cat. J. Biol Chem. 269(45):28514. 21 (1594); Techne, 275(21):1632-8 (2000), Lin. highly preferred indications are complications are complications assay transferred and include and inclu					polypeptides of the invention (including	skin), carpal tunnel syndrome and Dupuytren's
the invention) include assays disclosed infration in cheesity, additional highly operated infrations in 27(23)-14285-27 (1998); Mora. S. et al., 1810 (Chem. 269(45),2851-1 (1994); "Identification of a 30-base pair regulatory element and novel) DNA binding protein that regulates the human GLUT4 promoter in transgenic mice.", 1 Biol Chem. 2600 (1994); "Identification of a 30-base pair regulatory element and novel) DNA binding protein that regulates the human GLUT4 promoter in transgenic mice.", 1 Biol Chem. 2000 (1994); "Identification of a 30-base pair regulatory element and novel) for the second of the second of which is herein contains a contain of each of which is herein contains of each of which is herein microprorated by reference in its entirety. Adipocytes and appreadate A Exemplary cells that may be used according to these assays are publicly used according to these assays are publicly available (e.g., through the ATCO) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCO) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCO) and/or may be continuous substant of 373 fibroblasts developed through closal isolation. These cells undergo a pre-adipocyte to adipose-like conversion of the maximal publics, and an anagonists thereof) in detection, diagnosits, and stream of inflammation, Vascular Disea invention (including antibodies and apprendices of the invention (including antibodies and apprendic properties of the invention of the appearance) to adipose agains the adipose of the purporation of the invention of the appearance of the invention of the purporation of the anador returnent of Inflammation, Vascular Disea apprendices of the invention of the appearance of the appearan					antibodies and agonists or antagonists of	contracture). An additional highly preferred
in That, M.Y., et al., J. Biol Chem. 27(32):14285-52 (1998), Monz. S., et al. Biol Chem. 278(21):1632-8 (2000); Liu, M.L., et al., J. Biol Chem. 278(21):1632-8 (2000); Liu, M.L., et al., J. Biol Chem. 278(21):1632-8 (2000); Liu, Biol Chem. 2000, May 2425(3):2814- 21 (1993); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLITPA promoter in transgenic mice." J Biol Chem. 2000, May 2425(31):2366- 73; Barger, et al., Gene 66.1-10 (1988); and Chlella, B., et al., Methods in Enzymol. 2165-2-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocyte generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the art and may be used according to these assays are publicly available (e.g., through the art and may be used according to these assays are publicly available (e.g., through the art and may be used according to these assays are publicly available (e.g., through the art and may be used according to the art and managemists thereof) in detection, diagnosis, preve cells undergo a pre-adipocyte to adjoose- like conversion under appropriate differentiation outlure conditions. Production of ICAM-1 CAM-1 are well-known in the art and managemists thereof) in detection, diagnosis, and stepset through or produced on the art and managemists thereof) in detection, diagnosis, and stepset throughty or analysing a produced through a produced through a produced through the art and managemists thereof) in detection, diagnosis, and seeses the ability of polypeptides of the invention of transmitted against a produced through and a produced through a produced through a produced through a produced through a					the invention) include assays disclosed	indication is obesity and/or complications associated with
1 Biol Chem, 275(23)-1,4285-92 (1998). Mora, S. et al., M.L. et al., Biol Chem, 275(201)-1,1632-95 (2000), Liu, M.L. et al., Biol Chem, 2004-1, Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice*, 1 Biol Chem, 2000 Aug 4,275(31),2366- 73; Berger et al., Gene Goi10 (1988), and, Cullien, B. et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in senitrety. Adipocyses and pre-adipocytes that may be used according to these assays are publicly available (e.g., fungith Action and Action Chem, 2000) HHIGCS78 712 Production of ICAM-1 are well-known in the art and may be under appropriate differentiation culture conditions. HHIGCS78 712 Production of ICAM-1 are well-known in the art and may be used according to these assays for measuring expression of ICAM-1 are well-known in the art and may be used according to the assays for measuring expression of ICAM-1 are well-known in the art and may be used according to the assays for measuring expression of ICAM-1 are well-known in the art and may be used according to the assays for measuring expression of ICAM-1 are well-known in the art and may be used a routinely analyted of an alterioris, and strate invention (inclinding antibodies of the invention of antibodies, agon may be used a routinely antibodies and and advention, diagnosis, prevent assays include the well-known in the art and may be used a routinely antibodies of the invention of antibodies, agon are adveloped through colleges of the invention of antibodies, agon are adveloped through colleges of the invention of antibodies, agon are adveloped through colleges of the invention of antibodies, agon and agonists or antiagonists of the invention of sources or routinely more and or routinely and a productions. Athereosclerosis, Restencisis, and Stroke		-			inThai, M.V., et al., J Biol Chem,	obesity. Additional highly preferred indications include
High Chem, 275(21):16323-8 (2000); Liu, M.L., et al., 1810 Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem, 2000 Aug 42:75(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell sine which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposetile may be used or routinely modified to assess the ability of polypeptides of the invention) to agonists or antagonists of the invention) to					273(23):14285-92 (1998); Mora, S., et al.,	weight loss or alternatively, weight gain. Aditional
M.L., et al., J Biol Chem, 269(45):28514- 21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Eraymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adhocytes and pre-adhocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays and or may be used according to these assays and and assays include the mouse preadipocyte cell line. Mutich is an adherent mouse preadipocyte cell line whitch is an adherent mouse preadipocyte cell line whiteh is an adherent mouse preadipocyte of its conversion under appropriate differentiation culture conditions. HHGCS78 T12 Production of ICAM-1 Assays for measuring expression of ICAM-1 Assays for measuring expression of may be used or routinely modified to assess the ability of polypeptides of the invention) to		-			J Biol Chem, 275(21):16323-8 (2000); Liu,	highly preferred indications are complications associated
21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUTing protein that ranges for each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell incompleting to the each assays include the mouse 3T3-L1 cell incompleting to the each assays include the mouse 3T3-L1 cell incompleting and according to the invention (including antibodies and agonists of the invention) to					M.L., et al., J Biol Chem, 269(45):28514-	with insulin resistance.
regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4,275(31):23666- 73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incoprorated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 373-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 373-L1 cells are a continuous substrain of 373 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose- like conversion under appropriate differentiation culture conditions. HHGCS78 712 Production of ICAM-1 Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to					21 (1994); "Identification of a 30-base pair	
binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Breger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions HHGCS78 712 Production of ICAM-1 Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention) to agenists or antagonists of the invention) to					regulatory element and novel DNA	
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HHGCS78 712 Production of ICAM-1 Assays for measuring expression of ICAM-1 are well-known in the art and ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to					differentiation culture conditions.	
	198	HHGCS78	712	_	Assays for measuring expression of	Preferred embodiments of the invention include using
					ICAM-1 are well-known in the art and	polypeptides of the invention (or antibodies, agonists, or
					may be used or routinely modified to	antagonists thereof) in detection, diagnosis, prevention,
					assess the ability of polypeptides of the	and/or treatment of Inflammation, Vascular Disease,
\dashv					invention (including antibodies and	Athereosclerosis, Restenosis, and Stroke
					agonists or antagonists of the invention) to	

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				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
100	ниспти	713	Activition of	Account for the estimation of transmission	A management of the contraction
661	0717DUU	/13	Acuvation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Kesponse Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,

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				publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below and as the property of the prop
700	HHPFU28	714	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate breast lung colon prancearic escorbarged

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				assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, mentrophilis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
200 HH	HHPFU28	714	Activation of Endothelial Cell ERK Signaling Pathway.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Berra et al., Biochem Pharmacol 60(8):1171-1178 (2000); Gupta et al., Exp Cell Res 247(2):495-504 (1999); Chang and Karin, Nature 410(6824):37-40	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell differentiation. An method for stimulating endothelial cell differentiation.

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alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell differentiation. A highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac himself or the invention includes a method for reducing cardiac himself or the invention includes a method for reducing cardiac	of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabatic nearbroaday, intraordiac churt cardion.	hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that	Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, slymphangiosarcoma. Highly preferred indications also
(2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human imbilical vein endothelial	cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	·	·

	include cancers such as, prostate, breast, lung, colon,
	 pancreatic, esophageal, stomach, brain, liver, and urinary
	 cancer. Preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia. Highly preferred indications also include
	arterial disease, such as, atherosclerosis, hypertension,
	coronary artery disease, inflammatory vasculitides,
	Reynaud's disease and Reynaud's phenomenom,
	aneurysms, restenosis; venous and lymphatic disorders
	such as thrombophlebitis, lymphangitis, and lymphedema;
	and other vascular disorders such as peripheral vascular
	disease and cancer Highly preferred indications also
	include trailma such as wounds blirns and injured tissue
	(o & months intimated to intimate the internal forms from the forms forms
	(e.g., vascular injury such as, injury resulting from balloon
	angioplasty, and atheroschlerotic lesions), implant
	fixation, scarring, ischemia reperfusion injury, rheumatoid
	arthritis, cerebrovascular disease, renal diseases such as
	acute renal failure, and osteoporosis. Additional highly
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 	diabetic or other retinopathies, thrombotic and coagulative
	disorders, vascularitis, lymph angiogenesis, sexual
·····	disorders, age-related macular degeneration, and treatment
	/prevention of endometriosis and related conditions.
	Additional highly preferred indications include fibromas,
	heart disease, cardiac arrest, heart valve disease, and
	vascular disease. Preferred indications include blood
	SS
	Activity", "Blood-Related Disorders", and/or
	"Cardiovascular Disorders"). Preferred indications include
	autoimmune diseases (e.g., rheumatoid arthritis, systemic
	lupus erythematosis, multiple sclerosis and/or as described
	below) and immunodeficiencies (e.g., as described below).
	Additional preferred indications include inflammation and
	inflammatory disorders (such as acute and chronic
	inflammatory diseases, e.g., inflammatory bowel disease
	and Crohn's disease), and pain management.

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201 HHPSA85	715	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
		ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
		Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
			and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
-			assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
			invention (including antibodies and	differentiation. An alternative highly preferred
			agonists or antagonists of the invention) to	embodiment of the invention includes a method for
			promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
			activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
			assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
-			used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
			kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
			the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
			agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
			include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
	-		al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
			(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
			Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
	•		(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
			64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
			410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
			Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
			(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
		1	herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
			entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
			be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
			publicly available (e.g., through the	described below under "Infectious Disease").
			ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
			that may be used according to these assays	additional highly preferred indication is a complication
			include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
			adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
			is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
			cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
			and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
			like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
			differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or

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					blood vessel blockage), seizures, mental confusion,
					arowsiness, nonketotic hyperglycemic-hyperosmolar
					collia, calulovasculai ulsease (e.g., licari ulsease,
					stroke, and other diseases and disorders as described in the
					"Cardiovascular Disorders" section below), dyslipidemia,
					endocrine disorders (as described in the "Endocrine
					Disorders" section below), neuropathy, vision impairment
					(e.g., diabetic retinopathy and blindness), ulcers and
					impaired wound healing, infection (e.g., infectious
					diseases and disorders as described in the "Infectious
					Diseases" section below (particularly of the urinary tract
					and skin). An additional highly preferred indication is
					obesity and/or complications associated with obesity.
					Additional highly preferred indications include weight loss
					or alternatively, weight gain. Additional highly
					plicat
					insulin resistance. Additional highly preferred
					indications are disorders of the musculoskeletal systems
					including myopathies, muscular dystrophy, and/or as
					described herein. Additional highly preferred
					indications include, hypertension, coronary artery disease,
					dyslipidemia, gallstones, osteoarthritis, degenerative
					arthritis, eating disorders, fibrosis, cachexia, and kidney
					diseases or disorders. Preferred indications include
					neoplasms and cancer, such as, lymphoma, leukemia and
					breast, colon, and kidney cancer. Additional preferred
	•				indications include melanoma, prostate, lung, pancreatic,
					esophageal, stomach, brain, liver, and urinary cancer.
					Highly preferred indications include lipomas and
					liposarcomas. Other preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
					dysplasia.
202	HHSB106	716	Regulation of apoptosis	Caspase Apoptosis. Assays for caspase	A highly preferred indication is diabetes mellitus.
			in pancreatic beta cells.	apoptosis are well known in the art and	An additional highly preferred indication is a complication
				may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,

described in the "Renal Disorders" section below), diabetic stroke, and other diseases and disorders as described in the Diseases" section below, especially of the urinary tract and diabetic neuropathy), blood vessel blockage, heart disease, Disorders" section below), neuropathy, vision impairment neuropathy, nerve disease and nerve damage (e.g., due to indication is obesity and/or complications associated with "Cardiovascular Disorders" section below), dyslipidemia, highly preferred indications are complications associated obesity. Additional highly preferred indications include diabetic nephropathy, kidney disease (e.g., renal failure, impaired wound healing, and infection (e.g., infectious stroke, impotence (e.g., due to diabetic neuropathy or diseases and disorders as described in the "Infectious atherosclerosis, microvascular disease, hypertension, drowsiness, nonketotic hyperglycemic-hyperosmolar (e.g., diabetic retinopathy and blindness), ulcers and endocrine disorders (as described in the "Endocrine nephropathy and/or other diseases and disorders as blood vessel blockage), seizures, mental confusion, An additional highly preferred coma, cardiovascular disease (e.g., heart disease, skin), carpal tunnel syndrome and Dupuytren's weight loss or alternatively, weight gain. with insulin resistance. contracture). agonists or antagonists of the invention) to routinely modified to test capase apoptosis al., Br J Pharmacol, 129(4):687-94 (2000); apoptosis. Apoptosis in pancreatic beta is entirety. Pancreatic cells that may be used associated with induction and progression FEBS Lett, 459(2):238-43 (1999); Zhang, Harlan, J Atheroscler Thromb 3(2): 75-80 available (e.g., through the ATCC) and/or 39(6):1229-36 (1996); Krautheim, A., et ::S44-7 (2001); Suk K, et al., J Immunol, (1996); the contents of each of which are according to these assays include RIN-m. activity of polypeptides of the invention antagonists of the invention) include the may be routinely generated. Exemplary adiation induced transplantable rat islet FEBS Lett, 400(3):285-8 (1997); Saini, RIN-m is a rat adherent pancreatic beta assess the ability of polypeptides of the 37(3): 209-218 (2000); and Karsan and cell insulinoma cell line derived from a assays disclosed in: Loweth, AC, et al., 166(7):4481-9 (2001); Tejedo J, et al., (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res herein incorporated by reference in its caspase apoptosis that may be used or according to these assays are publicly including antibodies and agonists or Chandra J, et al., Diabetes, 50 Suppl promote caspase protease-mediated of diabetes. Exemplary assays for S., et al., FEBS Lett, 455(3):315-20 invention (including antibodies and KS, et al., Biochem Mol Biol Int, pancreatic cells that may be used

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				cell tumor. The cells produce and secrete islet polypeptide hormones, and produce	
				insulin, somatostatin, and possibly	
				glucagon. A1 IC: #CKL-205/ Cnick et al. Proc. Natl. Acad. Sci. 1977 74:628;	
				AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	
203	HHSB165	717	Production of ICAM-1	Assays for measuring expression of	Preferred embodiments of the invention include using
			-	ICAM-1 are well-known in the art and	polypeptides of the invention (or antibodies, agonists, or
				may be used or routinely modified to	antagonists thereof) in detection, diagnosis, prevention,
				assess the ability of polypeptides of the	and/or treatment of Vascular Disease, Atherosclerosis,
				invention (including antibodies and	Restenosis, Stroke, and Asthma.
				agonists or antagonists of the invention) to	
				regulate ICAM-1 expression. Exemplary	
				assays that may be used or routinely	
				modified to measure ICAM-1 expression	
				include assays disclosed in: Rolfe BE, et	
				al., Atherosclerosis, 149(1):99-110 (2000);	
				Panettieri RA Jr, et al., J Immunol,	
		_		154(5):2358-2365 (1995); and, Grunstein	
				MM, et al., Am J Physiol Lung Cell Mol	
				Physiol, 278(6):L1154-L1163 (2000), the	
				contents of each of which is herein	
				incorporated by reference in its entirety.	
				Cells that may be used according to these	
		-		assays are publicly available (e.g., through	
				the ATCC) and/or may be routinely	
				generated. Exemplary cells that may be	
				used according to these assays include	
				Aortic Smooth Muscle Cells (AOSMC);	
				such as bovine AOSMC.	
203	HHSB165	717	Regulation of apoptosis	Caspase Apoptosis. Assays for caspase	A highly preferred indication is diabetes mellitus.
			in pancreatic beta cells.	apoptosis are well known in the art and	An additional highly preferred indication is a complication
				may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,
				assess the ability of polypeptides of the	diabetic nephropathy, kidney disease (e.g., renal failure,
				invention (including antibodies and	nephropathy and/or other diseases and disorders as
				agonists or antagonists of the invention) to	described in the "Renal Disorders" section below), diabetic

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promote caspase protease-mediated	neuropathy, nerve disease and nerve damage (e.g., due to
apoptosis. Apoptosis in pancreatic beta is	diabetic neuropathy), blood vessel blockage, heart disease,
associated with induction and progression	stroke, impotence (e.g., due to diabetic neuropathy or
of diabetes. Exemplary assays for	blood vessel blockage), seizures, mental confusion,
caspase apoptosis that may be used or	drowsiness, nonketotic hyperglycemic-hyperosmolar
routinely modified to test capase apoptosis	coma, cardiovascular disease (e.g., heart disease,
activity of polypeptides of the invention	atherosclerosis, microvascular disease, hypertension,
(including antibodies and agonists or	stroke, and other diseases and disorders as described in the
antagonists of the invention) include the	"Cardiovascular Disorders" section below), dyslipidemia,
assays disclosed in: Loweth, AC, et al.,	endocrine disorders (as described in the "Endocrine
FEBS Lett, 400(3):285-8 (1997); Saini,	Disorders" section below), neuropathy, vision impairment
KS, et al., Biochem Mol Biol Int,	(e.g., diabetic retinopathy and blindness), ulcers and
39(6):1229-36 (1996); Krautheim, A., et	impaired wound healing, and infection (e.g., infectious
al., Br J Pharmacol, 129(4):687-94 (2000);	diseases and disorders as described in the "Infectious
Chandra J, et al., Diabetes, 50 Suppl	Diseases" section below, especially of the urinary tract and
1:S44-7 (2001); Suk K, et al., J Immunol,	skin), carpal tunnel syndrome and Dupuytren's
166(7):4481-9 (2001); Tejedo J, et al.,	contracture). An additional highly preferred
FEBS Lett, 459(2):238-43 (1999); Zhang,	besit
S., et al., FEBS Lett, 455(3):315-20	obesity. Additional highly preferred indications include
(1999); Lee et al., FEBS Lett 485(2-3):	weight loss or alternatively, weight gain. Aditional
122-126 (2000); Nor et al., J Vasc Res	highly preferred indications are complications associated
37(3): 209-218 (2000); and Karsan and	with insulin resistance.
Harlan, J Atheroscler Thromb 3(2): 75-80	
 (1996); the contents of each of which are	
herein incorporated by reference in its	
entirety. Pancreatic cells that may be used	
according to these assays are publicly	
available (e.g., through the ATCC) and/or	
may be routinely generated. Exemplary	
pancreatic cells that may be used	
according to these assays include RIN-m.	
RIN-m is a rat adherent pancreatic beta	
cell insulinoma cell line derived from a	
radiation induced transplantable rat islet	
cell tumor. The cells produce and secrete	
islet polypeptide hormones, and produce	
insulin, somatostatin, and possibly	

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				glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	
204	HHSDI53	718	Activation of transcription through serum response element in immune cells (such	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routingly modified to assess the	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the
				ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate	increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate the expression of genes involved in	"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for transcription through the SRE that may be	systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies
				activity of the polypeptides of the invention (including antibodies and	immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the	under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and
- -				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				cells that may be used according to these	metanoma, gltoma (e.g., malignant gltoma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that	stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and
				may be used according to these assays include the CTLL cell line, which is an II.	pre-neoplastic conditions, such as, for example, hyperplasia metaplasia and/or dysplasia. Preferred
		,		2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma.
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,

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					neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
504	HHSDI53	718	Production of IL-5	IL-5 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells, mast cells, basophils, and eosinophils that stimulate eosinophil function and B cell Ig production and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cell function, modulate B cell Ig production, modulate immune of polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-5, and the stimulation of eosinophil function and B cell Ig production. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-5 production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-5 production. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) immunoglobulin production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) immunoglobulin production. A highly preferred indication includes altergy. A highly preferred indication includes asthma. A highly preferred indication includes rhinitis. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred
				in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Ohshima et al.,	indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include

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-				Blood 92(9):338-3345 (1998); Jung et al., Eur J Immunol 25(8):2413-2416 (1995); Mori et al., J Allergy Clin Immunol 106(1 Pt 2):558-564 (2000); and Koning et al., Cytokine 9(6):427-436 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to	benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
205	HHSFC09	719	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, immunodeficiency (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional preferred indications include

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idiopathic pulmonary fibrosis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic
humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunicatured.	HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+ T cells. Deregulation of MHC class II has been associated with autoimmune diseases (e.g., diabetes, rheumatoid arthritis,
	Upregulation of HLA-DR and activation of T cells
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	systemic lupus et yurematosis, and munipre	Tupus et yunematosis, inimitipie scierosis and/or as described
	Scienosis, Assays for infinitionionidatory	below) and immunodeficiencies (e.g., as described below),
	proteins expressed on MFIC class II	boosting a 1 cell-mediated immune response, and
	expressing 1 cells and antigen presenting	ely, suj
	cells are well known in the art and may be	
	used or routinely modified to assess the	mellitus. An additional highly preferred indication
	ability of polypeptides of the invention	is a complication associated with diabetes (e.g., diabetic
	(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
	antagonists of the invention) to modulate	renal failure, nephropathy and/or other diseases and
	the activation of T cells, and/or mediate	disorders as described in the "Renal Disorders" section
	humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
	Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
	immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
	upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
	such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
	activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
	be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
-	immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as
	polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
	antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
	the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
	assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
	Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
	Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
	approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
	Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
	89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
	Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
	Gansbacher and Zier, Cell Immunol	complications associated with obesity. Additional highly
	117(1):22-34 (1988); and Itoh et al., J	preferred indications include weight loss or alternatively,
	Histochem Cytochem 40(11):1675-1683,	weight gain. Aditional highly preferred indications
	the contents of each of which are herein	are complications associated with insulin resistance.
	incorporated by reference in its entirety.	Additional highly preferred indications are disorders of the
	Human T cells that may be used according	musculoskeletal systems including myopathies, muscular
	to these assays may be isolated using	dystrophy, and/or as described herein.
	techniques disclosed herein or otherwise	additional preferred indication is infection (e.g., AIDS,
	known in the art. Human T cells are	and/or as described below under "Infectious Disease").

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Preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and allergy.	
primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the
	Regulation of viability and proliferation of pancreatic beta cells.
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				agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
207	HILCA24	721	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element that may be	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred

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				polypeptides of the invention (including	indications include neoplasms and cancers, such as,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and prostate, breast,
-				the invention) include assays disclosed in	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Berger et al., Gene 66:1-10 (1998); Cullen	and urinary cancer. Other preferred indications include
				and Malm, Methods in Enzymol 216:362-	benign dysproliferative disorders and pre-neoplastic
				368 (1992); Henthorn et al., Proc Natl	conditions, such as, for example, hyperplasia, metaplasia,
				Acad Sci USA 85:6342-6346 (1988);	and/or dysplasia. Preferred indications include
				Georas et al., Blood 92(12):4529-4538	anemia, pancytopenia, leukopenia, thrombocytopenia,
				(1998); Moffatt et al., Transplantation	Hodgkin's disease, acute lymphocytic anemia (ALL),
				69(7):1521-1523 (2000); Curiel et al., Eur	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				J Immunol 27(8):1982-1987 (1997); and	arthritis, AIDS, granulomatous disease, inflammatory
				Masuda et al., J Biol Chem	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				275(38):29331-29337 (2000), the contents	suppression of immune reactions to transplanted organs
				of each of which are herein incorporated	and tissues, hemophilia, hypercoagulation, diabetes
				by reference in its entirety. T cells that	mellitus, endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays are	An additional preferred indication is infection (e.g., an
				publicly available (e.g., through the	infectious disease as described below under "Infectious
				ATCC). Exemplary T cells that may be	Disease").
				used according to these assays include the	
				HT2 cell line, which is an IL-2 dependent	
				suspension culture of T cells that also	
				respond to IL-4.	
207 HII	HILCA24	721	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy.
	1 30		transcription through	through the Signal Transducers and	Another highly preferred indication is asthma.
			STAT6 response	Activators of Transcription (STAT6)	Additional highly preferred indications include
			element in immune	response element are well-known in the art	inflammation and inflammatory disorders.
			cells (such as T-cells).	and may be used or routinely modified to	Preferred indications include blood disorders (e.g., as
				assess the ability of polypeptides of the	described below under "Immune Activity", "Blood-
				invention (including antibodies and	Related Disorders", and/or "Cardiovascular Disorders").
				agonists or antagonists of the invention) to	Preferred indications include autoimmune diseases (e.g.,
				regulate STAT6 transcription factors and	rheumatoid arthritis, systemic lupus erythematosis,
				modulate the expression of multiple genes.	multiple sclerosis and/or as described below) and
				Exemplary assays for transcription through	immunodeficiencies (e.g., as described below).
				the STAT6 response element that may be	Preferred indications include neoplastic diseases (e.g.,
				used or routinely modified to test STAT6	leukemia, lymphoma, melanoma, and/or as described
				response element activity of the	below under "Hyperproliferative Disorders"). Preferred
				polypeptides of the invention (including	indications include neoplasms and cancers, such as,

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			antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents	leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to
			by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
 HII.CA24	722	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine

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				invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
208	HILCA24	722	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element that may be used or routinely modified to test STAT6 response element that may be	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred

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				polypeptides of the invention (including	indications include neoplasms and cancers, such as,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and prostate, breast,
				the invention) include assays disclosed in	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Berger et al., Gene 66:1-10 (1998); Cullen	and urinary cancer. Other preferred indications include
				and Malm, Methods in Enzymol 216:362-	benign dysproliferative disorders and pre-neoplastic
				368 (1992); Henthorn et al., Proc Natl	conditions, such as, for example, hyperplasia, metaplasia,
		•		Acad Sci USA 85:6342-6346 (1988);	and/or dysplasia. Preferred indications include
				Georas et al., Blood 92(12):4529-4538	anemia, pancytopenia, leukopenia, thrombocytopenia,
				(1998); Moffatt et al., Transplantation	Hodgkin's disease, acute lymphocytic anemia (ALL),
				69(7):1521-1523 (2000); Curiel et al., Eur	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
			·	J Immunol 27(8):1982-1987 (1997); and	arthritis, AIDS, granulomatous disease, inflammatory
			•	Masuda et al., J Biol Chem	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
	-			275(38):29331-29337 (2000), the contents	suppression of immune reactions to transplanted organs
				of each of which are herein incorporated	and tissues, hemophilia, hypercoagulation, diabetes
				by reference in its entirety. T cells that	mellitus, endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays are	An additional preferred indication is infection (e.g., an
				publicly available (e.g., through the	infectious disease as described below under "Infectious
				ATCC). Exemplary T cells that may be	Disease").
				used according to these assays include the	
				HT2 cell line, which is an IL-2 dependent	
				suspension culture of T cells that also	
				respond to IL-4.	
208 I	HILCA24	722	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy.
			transcription through	through the Signal Transducers and	Another highly preferred indication is asthma.
			STAT6 response	Activators of Transcription (STAT6)	Additional highly preferred indications include
			element in immune	response element are well-known in the art	inflammation and inflammatory disorders.
			cells (such as T-cells).	and may be used or routinely modified to	Preferred indications include blood disorders (e.g., as
				assess the ability of polypeptides of the	described below under "Immune Activity", "Blood-
				invention (including antibodies and	Related Disorders", and/or "Cardiovascular Disorders").
				agonists or antagonists of the invention) to	Preferred indications include autoimmune diseases (e.g.,
				regulate STAT6 transcription factors and	rheumatoid arthritis, systemic lupus erythematosis,
•				modulate the expression of multiple genes.	multiple sclerosis and/or as described below) and
				Exemplary assays for transcription through	immunodeficiencies (e.g., as described below).
_				the STAT6 response element that may be	Preferred indications include neoplastic diseases (e.g.,
	_			used or routinely modified to test STAT6	leukemia, lymphoma, melanoma, and/or as described
	_			response element activity of the	below under "Hyperproliferative Disorders"). Preferred
				polypeptides of the invention (including	indications include neoplasms and cancers, such as,

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				antibodies and agonists or antagonists of	lenkemia lymphoma melanoma and prostate breast
				the invention) include assays disclosed in	ling colon nancreatic esophageal stomach hrain liver
	<u> </u>			Berger et al., Gene 66:1-10 (1998); Cullen	and urinary cancer. Other preferred indications include
				and Malm, Methods in Enzymol 216:362-	benign dysproliferative disorders and pre-neoplastic
				368 (1992); Henthorn et al., Proc Natl	conditions, such as, for example, hyperplasia, metaplasia,
				Acad Sci USA 85:6342-6346 (1988);	and/or dysplasia. Preferred indications
				Georas et al., Blood 92(12):4529-4538	include anemia, pancytopenia, leukopenia,
				(1998); Moffatt et al., Transplantation	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				69(7):1521-1523 (2000); Curiel et al., Eur	anemia (ALL), plasmacytomas, multiple myeloma,
				J Immunol 27(8):1982-1987 (1997); and	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				Masuda et al., J Biol Chem	disease, inflammatory bowel disease, sepsis, neutropenia,
				275(38):29331-29337 (2000), the contents	neutrophilia, psoriasis, suppression of immune reactions to
				of each of which are herein incorporated	transplanted organs and tissues, hemophilia,
				by reference in its entirety. T cells that	hypercoagulation, diabetes mellitus, endocarditis,
				may be used according to these assays are	meningitis, and Lyme Disease.
				publicly available (e.g., through the	preferred indication is infection (e.g., an infectious disease
				ATCC). Exemplary T cells that may be	as described below under "Infectious Disease").
				used according to these assays include the	
				SUPT cell line, which is a suspension	
				culture of IL-2 and IL-4 responsive T cells.	
506	HISAT67	723	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment

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antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J. 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Grantorinol, 13(8):1305-17 (1999); Schinizu, H., et al., Ann N Y Acad Sci, and additional highly preferred indications associated with S65:441-4 (1998); Olson, L.K., et al., indication is obesity. Additional highly preferred indications associated with S65:441-4 (1998); Olson, L.K., et al., indication is obesity. Additional highly preferred indications associated with Soreening, 4:193-204 (1999), the contents of each of which is herein incorporated by creference in its entirety. Pancreatic cells that may be used according to these assays include HITIT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells ransformed with SV40. These cells express glucagon, somatostatin, and glucose and glucagon and suppressed by somatostatin or glucose and glucagon and suppressed by somatostatin or Sci. USA 78: 4339-433, 1981.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and
antibodies and agonists or antagonist the invention) include assays disclos Shimizu, H., et al., Endocr J, 47(3): (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad 865:441-4 (1998); Olson, L.K., et al Biol Chem, 271(28):16544-52 (1999) Miraglia S et. al., Journal of Biomol Screening, 4:193-204 (1999), the co of each of which is herein incorpora reference in its entirety. Pancreatic that may be used according to these are publicly available (e.g., through ATCC) and/or may be routinely gen Exemplary pancreatic cells that may used according to these assays inclu HITT15 Cells. HITT15 are an adhe epithelial cell line established from hamster islet cells transformed with These cells express glucagon, somatostatin, and glucocorticoid rec The cells secrete insulin, which is stimulated by glucose and glucagon suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. 547-551; Santerre et al. Proc. Natl. Sci. USA 78: 4339-4343, 1981.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and
	Regulation of viability and proliferation of pancreatic beta cells.
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				example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
	-			viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
				regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
			-	invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
				agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
				include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
	,			BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
				(2001); Huotari MA, et al., Endocrinology,	skin), carpal tunnel syndrome and Dupuytren's
				139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
				Biol Chem 1998 Jul 10;273(28):17771-9	obesit
		• • • •		(1998), the contents of each of which is	obesity. Additional highly preferred indications include
				herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
				entirety. Pancreatic cells that may be used	tions ass
				according to these assays are publicly	with insulin resistance.
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
	·			X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
211	HJMAA03	725	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications

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				(including antibodies and agonists or	include blood disorders (e.g. as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
• • •				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
		-			meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
211	HJMAA03	725	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication

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	patiercatic octa cells.	of fourtifiery induffice to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
		or polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
		antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
		the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
		secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
		is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
		insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
		pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
-		glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
		proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
		key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
		assays that may be used or routinely	stroke, and other diseases and disorders as described in the
		modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
		secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
		polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
		antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
		the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
		Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
		2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
		Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
		Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
		(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
	_	Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
		(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
		herein incorporated by reference in its	highly preferred indications are complications associated
		entirety. Pancreatic cells that may be used	with insulin resistance.
		according to these assays are publicly	
		available (e.g., through the ATCC) and/or	
		may be routinely generated. Exemplary	
		pancreatic cells that may be used	
		according to these assays include rat INS-1	
		cells. INS-1 cells are a semi-adherent cell	
		line established from cells isolated from an	
		X-ray induced rat transplantable	
		insulinoma. These cells retain	
		characteristics typical of native pancreatic	
		beta cells including glucose inducible	

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				insulin secretion. References: Asfari et al.	
212	HJMAV41	726	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
	i				transplanted organs and tissues, hemophilia,

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					hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
212	HJMAV41	726	Production of TNF alpha by T cells	INFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts,	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred
				exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of	stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),
				polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate invention) to mediate	Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described helow) immunodeficiencies (e.g., as described below)
				inflammation and cytotoxicity, and mediate humoral and/or cell-mediated immunity. Exemplary assays that test for	boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include
				immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that	inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under
				may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in	"Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and
				Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapte 6:138-160 (2000); Verhasselt et	urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia,
				a., Eul J minumo 26(11):3660-3690 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et	pancytopenia, ieukopenia, inrombocytopenia, Hodgkin s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, asthma,

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				al., J Immunol 138:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to	ALDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
213	НЈМАҮ90	727	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and

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				incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through	melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred	
				the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred	
				2 dependent suspension culture of T cells with cytotoxic activity.	indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic	
					anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous	
					disease, inflammatory bowel disease, neutropenia,	
					neducipinita, psortasis, suppression of immune reactions to transplanted organs and tissues, hemophilia,	
					hypercoagulation, diabetes mellitus, endocarditis,	
					meningitis, Lyme Disease, cardiac reperfusion injury, and	
					asunna and allergy. An additional preferred indication	
					is intection (e.g., an intectious disease as described below inder "Infections Disease")	
213	HJMAY90	727	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention	
					includes a method for stimulating (e.g., increasing) IL-6	
				_	production. An alternative highly preferred embodiment of	
					the invention includes a method for inhibiting (e.g.,	
					reducing) IL-6 production. A highly preferrred	
				uo uo	indication is the stimulation or enhancement of mucosal	
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood	
				, and	disorders (e.g., as described below under "Immune	
				Chronic hyperproliferative diseases.	Activity', "Blood-Related Disorders", and/or	
				ced by	Carulovasculai Disorders), and infection (e.g., as described below under "Infectious Disease") Hiohly	
					preferred indications include autoimmune diseases (e.g.,	
					rheumatoid arthritis, systemic lupus erythematosis,	
					multiple sclerosis and/or as described below) and	
				_	immunodeficiencies (e.g., as described below). Highly	
					preferred indications also include boosting a B cell-	
				<u> </u>	mediated immune response and alternatively suppressing a	
				r antagonists of	B cell-mediated immune response. Highly preferred	
				the invention) to mediate	indications include inflammation and inflammatory	− ₁

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				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
		***		immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
		· · · ·		Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
····				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
╅				proliferation and functional activities.	
214 HJ	HJPBE39	728	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune
			in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
			as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
	•			antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
				the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				transcription through the AP1 response	multiple sclerosis and/or as described below) and

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				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
			-	assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
				with cytotoxic activity.	
214	HJPBE39	728	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
			transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
			cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
			element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
			cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
				antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
				the invention) to increase cAMP and	arthritis, systemic lupus erythematosis, multiple sclerosis
				regulate CREB transcription factors, and	and/or as described below), immunodeficiencies (e.g., as
				modulate expression of genes involved in a	described below), boosting a T cell-mediated immune
				wide variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
				assays for transcription through the cAMP	response. Additional preferred indications include
				response element that may be used or	inflammation and inflammatory disorders. Highly
				routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under

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				invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T	"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
214	НРВЕЗ9	728	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response.

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				66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.	inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and
214	НРВЕЗ9	728	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below

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				85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
214	HJPBE39	728	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic

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					and anergy.
515	HJPBK28	729	Activation of	Assays for the activation of transcription	Highly preferred indications include inflammation and
			transcription through	through the NFKB response element are	inflammatory disorders. Highly preferred indications
			NFKB response	well-known in the art and may be used or	include blood disorders (e.g., as described below under
			element in immune	routinely modified to assess the ability of	"Immune Activity", "Blood-Related Disorders", and/or
			cells (such as T-cells).	polypeptides of the invention (including	"Cardiovascular Disorders"). Highly preferred indications
				antibodies and agonists or antagonists of	include autoimmune diseases (e.g., rheumatoid arthritis,
				the invention) to regulate NFKB	systemic lupus erythematosis, multiple sclerosis and/or as
				transcription factors and modulate	described below), and immunodeficiencies (e.g., as
				expression of immunomodulatory genes.	described below). An additional highly preferred
				Exemplary assays for transcription through	indication is infection (e.g., AIDS, and/or an infectious
				the NFKB response element that may be	disease as described below under "Infectious Disease").
			-	used or rountinely modified to test NFKB-	Highly preferred indications include neoplastic diseases
				response element activity of polypeptides	(e.g., melanoma, leukemia, lymphoma, and/or as described
				of the invention (including antibodies and	below under "Hyperproliferative Disorders"). Highly
				agonists or antagonists of the invention)	preferred indications include neoplasms and cancers, such
				include assays disclosed in Berger et al.,	as, melanoma, renal cell carcinoma, leukemia, lymphoma,
				Gene 66:1-10 (1998); Cullen and Malm,	and prostate, breast, lung, colon, pancreatic, esophageal,
				Methods in Enzymol 216:362-368 (1992);	stomach, brain, liver and urinary cancer. Other preferred
				Henthorn et al., Proc Natl Acad Sci USA	indications include benign dysproliferative disorders and
				85:6342-6346 (1988); Black et al., Virus	pre-neoplastic conditions, such as, for example,
				Gnes 15(2):105-117 (1997); and Fraser et	hyperplasia, metaplasia, and/or dysplasia. Preferred
		·····		al., 29(3):838-844 (1999), the contents of	indications also include anemia, pancytopenia, leukopenia,
				each of which are herein incorporated by	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				reference in its entirety. T cells that may	anemia (ALL), plasmacytomas, multiple myeloma,
				be used according to these assays are	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia,
		-		ATCC). Exemplary human T cells that	neutrophilia, psoriasis, hemophilia, hypercoagulation,
				may be used according to these assays	diabetes mellitus, endocarditis, meningitis, Lyme Disease,
				include the SUPT cell line, which is a	suppression of immune reactions to transplanted organs,
				suspension culture of IL-2 and IL-4	asthma and allergy.
,;	COLLOGIA			responsive T cells.	
216	HJPCH08	730	Proliferation,	Kinase assays, for example kinase assays	Preferred embodiments of the invention include using
			differentiation, and/or	for members of the MAP kinase family	polypeptides of the invention (or antibodies, agonists, or
			cytokine production in	(including p38, JAK, and ERK) are well	antagonists thereof) in detection, diagnosis, prevention,
			immune cells (such as	known in the art and may be used or	and/or treatment of inflammation, infection, allergy,
			I -cells).	routinely modified to assess the ability of	asthma, autoimmunity, and cancer.

			polypeptides of the invention (including	
			the invention) to promote or inhibit cell	
			proliferation, differentiation., and/or	
			cytokine production in immune cells such	
			as T-cells. Exemplary assays for MAP	
			kinase family members that may be used	
			or routinely modified to test polypeptides	
			of the invention (including antibodies and	
			agonists or antagonists of the invention)	
			include the assays disclosed in: Rincon M.,	
			Curr Opin Immunol; 13(3):339-345	
			(2001); Wang LH, et al., J Immunol,	
			162(7):3897-3904 (1999); Sakamoto H, et	
			al., J Biol Chem, 275(46):35857-35862	
			(2000), the contents of each of which are	
			herein incorporated by reference in its	
			entirety. Exemplary immune cells (for	
			example, T-cells) that may be used	
			according to these assays include the	
7			mouse CTLL cell line.	
217 HKABU43	731	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
		ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
		Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
			and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
			assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
			invention (including antibodies and	differentiation. An alternative highly preferred
			agonists or antagonists of the invention) to	embodiment of the invention includes a method for
			promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
			activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
			assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
			used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
			kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
			the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
			agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
			include the assays disclosed in Forrer et	described below under "Endocrine Disorders").

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al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic	
Endocrinol Diabetes 107(2):126-132	unseases (e.g., iipoliias, iiposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred	
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,	
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart	
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below	
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",	
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders	
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural	
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity	
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as	
publicly available (e.g., through the	described below under "Infectious Disease").	
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An	
that may be used according to these assays	additional highly preferred indication is a complication	
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,	
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,	
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as	
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic	
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to	
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,	
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or	
	blood vessel blockage), seizures, mental confusion,	
	drowsiness, nonketotic hyperglycemic-hyperosmolar	
	coma, cardiovascular disease (e.g., heart disease,	
	atherosclerosis, microvascular disease, hypertension,	
	stroke, and other diseases and disorders as described in the	
	"Cardiovascular Disorders" section below), dyslipidemia,	
-	endocrine disorders (as described in the "Endocrine	
	Disorders" section below), neuropathy, vision impairment	
	(e.g., diabetic retinopathy and blindness), ulcers and	
	impaired wound healing, infection (e.g., infectious	
	diseases and disorders as described in the "Infectious	
	sec	
	and skin). An additional highly preferred indication is	
	obesity and/or complications associated with obesity.	_
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	or alternatively, weight gain. Additional highly	_

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			Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and
218 HKACI79	732	Upregulation of CD152 and activation of T cells	expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hymernroliferative Disorders"), Additionally under "Hymernroliferative Disorders").

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highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, inflammation and inflammatory disorders, and asthma and allergy. An additional preferred indication is infection (e.g., as described below under "Infectious Disease").	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and
immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+ T cells. Deregulation of MHC class II has been associated with autoimmune diseases (e.g., diabetes, rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis). Assays for immunomodulatory proteins expressed on MHC class II
	Upregulation of HLA-DR and activation of T cells
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expressing T cells and antigen presenting	alternatively, suppressing a T cell-mediated immune
cells are well known in the art and may be	response. A highly preferred indication is diabetes
used or routinely modified to assess the	mellitus. An additional highly preferred indication
ability of polypeptides of the invention	is a complication associated with diabetes (e.g., diabetic
(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
antagonists of the invention) to modulate	renal failure, nephropathy and/or other diseases and
the activation of T cells, and/or mediate	disorders as described in the "Renal Disorders" section
humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as
polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
Gansbacher and Zier, Cell Immunol	complications associated with obesity. Additional highly
117(1):22-34 (1988); and Itoh et al., J	preferred indications include weight loss or alternatively,
Histochem Cytochem 40(11):1675-1683,	weight gain. Aditional highly preferred indications
 the contents of each of which are herein	are complications associated with insulin resistance.
incorporated by reference in its entirety.	Additional highly preferred indications are disorders of the
 Human T cells that may be used according	musculoskeletal systems including myopathies, muscular
to these assays may be isolated using	dystrophy, and/or as described herein.
techniques disclosed herein or otherwise	additional preferred indication is infection (e.g., AIDS,
known in the art. Human T cells are	and/or as described below under "Infectious Disease").
 primary human lymphocytes that mature in	Preferred indications include endocrine disorders (e.g., as
the thymus and express a T Cell receptor	described below under "Endocrine Disorders"), and
and CD3, CD4, or CD8. These cells	neoplastic diseases (e.g., leukemia, lymphoma, and/or as

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				mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and allergy.
219	HKAFF50	733	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and lacobelli, J Immunol 159(3):1319-1327	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. An

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				(1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	additional highly preferred indication includes infection (e.g., AIDS, and/or as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma, leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and uninary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is infection (e.g., tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or an eurotopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, thrombocytopenia, Hodgkin's disease, acute lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, nenophilia, hypercoagulation, diabetes mellitus, endocarditis, mennoptits I ymp preserventered indications and preserventered indications and preserventered indications and preserventered indications and preservented indications
219	HKAFF50	733	Upregulation of CD69 and activation of T cells	CD69 FMAT. CD69 is an activation marker that is expressed on activated T	and allergy. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative
				cells, B cells, and NK cells. CD69 is not	highly preferred embodiment of the invention includes a

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expressed on resting T cells. B cells, or	method for inhibiting the activation of and/or inactivating
NK cells. CD69 has been found to be	T cells. A highly preferred embodiment of the
associated with inflammation. Assays for	invention includes a method for activation B cells. An
immunomodulatory proteins expressed in	alternative highly preferred embodiment of the invention
T cells, B cells, and leukocytes are well	includes a method for inhibiting the activation of and/or
known in the art and may be used or	inactivating B cells. A highly preferred embodiment
routinely modified to assess the ability of	of the invention includes a method for activating NK cells.
polypeptides of the invention (including	An alternative highly preferred embodiment of the
antibodies and agonists or antagonists of	invention includes a method for inhibiting activation of
the invention) to modulate the activation of	and/or inactivation NK cells. Highly preferred
T cells, and/or mediate humoral or cell-	indications include inflammation and inflammatory
mediated immunity. Exemplary assays	disorders (e.g., as described below under "Immune
 that test for immunomodulatory proteins	Activity"). Preferred indications include blood
 evaluate the upregulation of cell surface	disorders (e.g., as described below under "Immune
markers, such as CD69, and the activation	Activity", "Blood-Related Disorders", and/or
of T cells. Such assays that may be used	"Cardiovascular Disorders"). Highly preferred indications
or routinely modified to test	include autoimmune diseases (e.g., rheumatoid arthritis,
 immunomodulatory activity of	systemic lupus erythematosis, multiple sclerosis and/or as
polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
 Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
 Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
Afetra et al., Ann Rheum Dis 52(6):457-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,
are herein incorporated by reference in its	neutrophilia, psoriasis, suppression of immune reactions to
entirety. Human T cells that may be used	transplanted organs and tissues, hemophilia,
according to these assays may be isolated	hypercoagulation, diabetes mellitus, endocarditis,
 using techniques disclosed herein or	meningitis, Lyme Disease, inflammation and
 otherwise known in the art. Human T cells	inflammatory disorders, asthma, and allergies.
are primary human lymphocytes that	Preferred indications also include neoplastic diseases (e.g.,

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				mature in the thymus and express a T Cell	leukemia, lymphoma, and/or as described below under
				receptor and CLD3, CLP4, or CLD3. These cells mediate humoral or cell-mediated	"Hyperproliterative Disorders"). Preferred indications include neonlasms such as for example lenkemia
				immunity and may be preactivated to	lymphoma, and prostate, breast, lung, colon, pancreatic,
				enhance responsiveness to	esophageal, stomach, brain, liver and urinary cancer.
				immunomodulatory factors.	Other preferred indications include benign dysproliferative
					disorders and pre-neoplastic conditions, such as, for
220	HKGBF25	734	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
ì		-	transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,

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				אונוו כלוניוטאור מכנועונץ.	unominocytopenia, modgam s disease, acute iymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
			_		disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
		,			transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
221	HKIXC44	735	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
			•	secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Shirnizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
				(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
				Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
				Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
				865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
				Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
				Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional

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omplications associated	ferred embodiment of the invention of for activating T cells. An alternative embodiment of the invention includes a niting the activation of and/or inactivating ighly preferred embodiment of the ess a method for activation B cells. An y preferred embodiment of the invention of for inhibiting the activation of and/or alls. A highly preferred embodiment includes a method for activating NK cells. Byly preferred embodiment of the ess a method for inhibiting activation of on NK cells. Highly preferred de inflammation and inflammatory s described below under "Immune Preferred indications include blood s described below under "Immune
highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for activation B cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating B cells. A highly preferred embodiment of the invention includes a method for activating NK cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting activation of and/or inactivation NK cells. Highly preferred indications include inflammation and inflammatory disorders (e.g., as described below under "Immune Activity"). Preferred indications include blood disorders (e.g., as described below under "Immune
Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	CD69 FMAT. CD69 is an activation marker that is expressed on activated T cells, B cells, and NK cells. CD69 is not expressed on resting T cells, B cells, or NK cells. CD69 has been found to be associated with inflammation. Assays for immunomodulatory proteins expressed in T cells, B cells, and leukocytes are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cellmediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface
	Upregulation of CD69 and activation of T cells
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				Total and the ODG	A 24: 14: 31 (10) (10) (10)
·				of T cells. Such assays that may be used	Activity, Diode-related Disolucis, alluful "Cardiovascular Disorders") Highly preferred indications
				or routinely modified to test	include autoimmune diseases (e.g., rheumatoid arthritis
				immunomodulatory activity of	systemic lupus erythematosis, multiple sclerosis and/or as
		-		polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
				antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
				the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
				assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
				Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
				Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
				approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
				Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
				(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
				(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
				Afetra et al., Ann Rheum Dis 52(6):457-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,
				are herein incorporated by reference in its	neutrophilia, psoriasis, suppression of immune reactions to
				entirety. Human T cells that may be used	transplanted organs and tissues, hemophilia,
				according to these assays may be isolated	hypercoagulation, diabetes mellitus, endocarditis,
				using techniques disclosed herein or	meningitis, Lyme Disease, inflammation and
				otherwise known in the art. Human T cells	inflammatory disorders, asthma, and allergies.
				are primary human lymphocytes that	Preferred indications also include neoplastic diseases (e.g.,
		•		mature in the thymus and express a T Cell	leukemia, lymphoma, and/or as described below under
				receptor and CD3, CD4, or CD8. These	"Hyperproliferative Disorders"). Preferred indications
				cells mediate humoral or cell-mediated	include neoplasms, such as, for example, leukemia,
				immunity and may be preactivated to	lymphoma, and prostate, breast, lung, colon, pancreatic,
•				enhance responsiveness to	esophageal, stomach, brain, liver and urinary cancer.
				immunomodulatory factors.	Other preferred indications include benign dysproliferative
					disorders and pre-neoplastic conditions, such as, for
					example, hyperplasia, metaplasia, and/or dysplasia.
223	HKMLM95	737	Production of	IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
					inclu
					of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune

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	macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
	MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
	immunomodulatory proteins produced by	
	T cells and NK cells that regulate a variety	ety granulomatosus disease and malignant osteoporosis,
	of inflammatory activities and inhibit TH2	
	helper cell functions are well known in the	the Highly preferred indications include autoimmune disease
	art and may be used or routinely modified	
	to assess the ability of polypeptides of the	
	invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
	agonists or antagonists of the invention) to	
	mediate immunomodulation, regulate	
	inflammatory activities, modulate TH2	indications include inflammation and inflammatory
	helper cell function, and/or mediate	disorders. Additional preferred indications include
	humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
	Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
	immunomodulatory proteins evaluate the	
	production of cytokines, such as Interferon	_
	gamma (IFNg), and the activation of T	
	cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
	routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
	immunomodulatory activity of	
	polypeptides of the invention (including	
	antibodies and agonists or antagonists of	
	the invention) include the assays disclosed	ed metaplasia, and/or dysplasia. Preferred indications
	in Miraglia et al., J Biomolecular	
	Screening 4:193-204 (1999); Rowland et	
	al., "Lymphocytes: a practical approach"	
	Chapter 6:138-160 (2000); Gonzalez et al.,	al., Burkitt's lymphoma, arthritis, AIDS, granulomatous
	J Clin Lab Anal 8(5):225-233 (1995);	
	Billiau et al., Ann NY Acad Sci 856:22-32	~
	(1998); Boehm et al., Annu Rev Immunol	
	15:749-795 (1997), and Rheumatology	
-	(Oxford) 38(3):214-20 (1999), the contents	
	of each of which are herein incorporated	
	by reference in its entirety. Human T cells	alls
	that may be used according to these assays	SÁ
	may be isolated using techniques disclosed	pas

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			herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to	
224 HKTAB41	738	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication
			of routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuronathy nerve disease and nerve damage (e.g., due to
			is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain	diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar
			proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by	coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine
			polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999);	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's
			Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by	contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer.
that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, differentiation, and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345 (2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakamoto H, et al., J Biol Chem, 275(46):35857-35862
	Proliferation, differentiation, and/or cytokine production in immune cells (such as T-cells).
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				(2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the mouse CTLL cell line.	
226	HLDCA54	740	Production of RANTES	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407 (1995), the contents of each of which are herein incorporated by reference in its entirety. Human immune	A highly preferred embodiment of the invention includes a method for stimulating RANTES production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) RANTES production. A highly preferred indication is infectious Disease"). A most highly preferred indication of HIV infectious disease as described below under "Infectious Disease"). A most highly preferred indication includes AIDS and/or the prevention or reduction of HIV infection. Additional highly preferred indication includes immune disorders, for example, inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, asthma, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disoaces").
				cells that may be used according to these	Highly preferred indications include neoplasms, such as,

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				assays may be isolated using techniques disclosed herein or otherwise known in the art.	for example, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
227 田	HLDQU79	741	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with insulin resistance. Alighly preferred indications are complications associated with insulin resistance.

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				according to these assays include rat INC-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
_				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
\dashv				Endocrinology 1992 130:167.	
227 H	нгрол29	741	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
•				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
	_			include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
•				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred

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				2 dependent suspension culture of T cells with cytotoxic activity.	indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
728	HLDRT09	742	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, and prostate, breast, lung, colon, pancreatic, esophageal,

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\				include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
229	HLHAP05	743	Regulation of transcription through the FAS promoter element in hepatocytes	Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct and to regulate transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This stimulation of transcription is also somewhat glucose dependent. Exemplary assays that may be used or routinely modified to test for FAS	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment

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				promoter element activity (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Xiong, S., et al., Proc Natl Acad Sci U.S.A., 97(8):3948-53 (2000); Roder, K., et al., Eur J Biochem, 260(3):743-51 (1999); Oskouian B, et al., Biochem J, 317 (Pt 1):257-65 (1996); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays, such as H4IIE cells, are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays include rat liver hepatoma cell line(s) inducible with glucocorticoids, insulin, or cAMP	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuyren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance.
230	HLHCS23	744	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dysligidemia.

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endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple
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endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impal (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectiou diseases and disorders as described in the "Infectiou Diseases" section below, especially of the urinary traskin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated obesity. Additional highly preferred indications incl weight loss or alternatively, weight gain. Adhiply preferred indications are complications associwith insulin resistance.	A preferred embodiment of the invention inclumethod for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred in include blood disorders (e.g., as described below "Immune Activity", "Blood-Related Disorders", a "Cardiovascular Disorders"), Highly preferred in include autoimmune diseases (e.g., rheumatoid ar systemic lupus erythematosis, Crohn's disease, mu
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endocrine disorders (as Disorders" section belo (e.g., diabetic retinopal impaired wound healin diseases and disorders Diseases" section belo skin), carpal tunnel syr contracture). An indication is obesity an obesity. Additional highly preferred indication with insulin resistance.	preferred for inh ction. An tion inclu ising) TN le blood cune Activune Activune Activune liovascula le autoim nic lupus
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regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ohtani KI, et al., Endocrinology, 139(1):172-8 (1998); Krautheim A, et al, Exp Clin Endocrinol Diabetes, 107 (1):29-34 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for
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	Activation of transcription through serum response element in immune cells (such as T-cells).
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				transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, thrombocytopenia, Hodgkin's disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meutrophilia, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
230	HLHCS23	744	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

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infections, tuberculosis, infections associated with chronic immunodeficiency (e.g., as described below), boosting a T brain, liver and urinary cancer. Other preferred indications neutrophilia, psoriasis, suppression of immune reactions to cell-mediated immune response, and suppressing a T cellthrombocytopenia, Hodgkin's disease, acute lymphocytic Highly preferred indications include autoimmune disease disease, inflammatory bowel disease, sepsis, neutropenia, (e.g., rheumatoid arthritis, systemic lupus erythematosis, mediated immune response. Additional highly preferred example, leukemia, lymphoma, melanoma, and prostate, neoplastic conditions, such as, for example, hyperplasia, lymphoma, melanoma, and/or as described below under indications include neoplasms and cancers, such as, for and/or as described below under "Infectious Disease"), indications include neoplastic diseases (e.g., leukemia, 'Cardiovascular Disorders"), and infection (e.g., viral Preferred indications granulomatosus disease and malignant osteoporosis, breast, lung, colon, pancreatic, esophageal, stomach, Burkitt's lymphoma, arthritis, AIDS, granulomatous disorders. Additional preferred indications include indications include inflammation and inflammatory anemia (ALL), plasmacytomas, multiple myeloma, "Hyperproliferative Disorders"). Highly preferred include benign dysproliferative disorders and preidiopathic pulmonary fibrosis. Highly preferred hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. multiple sclerosis and/or as described below). transplanted organs and tissues, hemophilia, include anemia, pancytopenia, leukopenia, metaplasia, and/or dysplasia. (Oxford) 38(3):214-20 (1999), the contents agonists or antagonists of the invention) to production of cytokines, such as Interferon helper cell functions are well known in the Chapter 6:138-160 (2000); Gonzalez et al., T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 by reference in its entirety. Human T cells may be isolated using techniques disclosed to assess the ability of polypeptides of the Billiau et al., Ann NY Acad Sci 856:22-32 that may be used according to these assays art and may be used or routinely modified the invention) include the assays disclosed immunomodulatory proteins produced by (1998); Boehm et al., Annu Rev Immunol immunomodulatory proteins evaluate the Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" antibodies and agonists or antagonists of polypeptides of the invention (including of each of which are herein incorporated inflammatory activities, modulate TH2 gamma (IFNg), and the activation of T 15:749-795 (1997), and Rheumatology cells. Such assays that may be used or mediate immunomodulation, regulate J Clin Lab Anal 8(5):225-233 (1995); helper cell function, and/or mediate humoral or cell-mediated immunity. herein or otherwise known in the art. invention (including antibodies and in Miraglia et al., J Biomolecular immunomodulatory activity of Exemplary assays that test for MHC expression. Assays for routinely modified to test

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				Human T cells are primary human lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
+				immunomodulatory factors.	
231	HLIBO72	745	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
	-			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
		_		Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic

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					anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
232	HLJCE88	746	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the sexpression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indication sinclude neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and indications include benign dysproliferative disorders and
					indications include benign dysproliferative disorders a pre-neoplastic conditions, such as, for example,

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232 HLICE88	746	Stimulation of insulin secretion from pancreatic beta cells.	include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity. Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt	hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, ALDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus, and additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, stroke, impotence (e.g., due to diabetic neuropathy or disease, and disorders (as described in the "Endocrine disorders (as described in the "Endocrine Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious
			2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of	Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with

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				herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	highly preferred indications are complications associated with insulin resistance.
233	HLICO10	747	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hymerroliferative Disorders") Additionally

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plasms and I Jymphoma, na), solid tumors, atic, esophageal, . Other preferred ive disorders and kample, a. Preferred a, leukopenia, cute lymphocytic myeloma, unulomatous utropenia, nmune reactions to nilia, ocarditis, fusion injury, and eferred indication s described below	NF alpha bodiment of the ing (e.g., eferred indications ed below under orders", and/or eferred indications matoid arthritis, sease, multiple munodeficiencies cell-mediated eferred indications disorders, and unmatoid arthritis.
highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, modition, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sensis
highly preferred indications cancers, such as, for exampl melanoma, glioma (e.g., ma and prostate, breast, lung, co stomach, brain, liver and ur indications include benign d pre-neoplastic conditions, st hyperplasia, metaplasia, and indications include anemia, thrombocytopenia, Hodgkin anemia (ALL), plasmacytom Burkitt's lymphoma, arthriti disease, inflammatory bowel neutrophilia, psoriasis, supp transplanted organs and tissu hypercoagulation, diabetes r meningitis, Lyme Disease, c asthma and allergy. An ais infection (e.g., an infection under "Infectious Disease").	A preferred method for inhi production. An invention includincreasing) TN include blood of "Immune Activo" "Cardiovascula include autoimus systemic lupus sclerosis and/or (e.g., as describi immune respon immune respon include inflamm treating joint da An additional h
Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998): Cullen and Malm.
Vir con inco cell assi the may incl incl with	Activation of transcription through throse serum response element (SR in immune cells (such abil abil abil abil apil abil abil apil abil apil abil apil abil apil abil apil apil apil apil apil apil apil ap
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Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infections Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., AIDS). Preferred indications include boosting a Total mediatal immunodeficiencies (e.g., AIDS).
Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	CD154 FMAT. CD154 (a.k.a., CD40L) expression is induced following activation of T cells. Interraction between CD154 and CD40 on B cells is required for correct antibody class switching and germinal center formation. Mutations in CD154 are linked to immunodeficiencies and increased susceptibility to infections. Assays for immunomodulatory proteins important for antibody class switching and TH1 function and expressed on activated T helper lymphocytes are well known in the art and may be used or routinely modified to assess the ability of polymentides of the
	Upregulation of CD154 and activation of T cells
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				invention (including antibodies and	alternatively, suppressing a T cell-mediated immune
				agonists or antagonists of the invention) to	response. Preferred indications include neoplastic
				modulate the activation of T cells,	diseases (e.g., leukemia, lymphoma, and/or as described
		-		modulate antibody class switching,	below under "Hyperproliferative Disorders"). Highly
				mediate TH1 function, and/or mediate	preferred indications include neoplasms, such as, for
				humoral or cell-mediated immunity.	example, leukemia, lymphoma, and prostate, breast, lung,
				Exemplary assays that test for	colon, pancreatic, esophageal, stomach, brain, liver and
				immunomodulatory proteins evaluate the	urinary cancer. Other preferred indications include benign
				upregulation of cell surface markers, such	dysproliferative disorders and pre-neoplastic conditions,
				as CD154, and the activation of T cells.	such as, for example, hyperplasia, metaplasia, and/or
				Such assays that may be used or routinely	dysplasia. Preferred indications also include anemia,
				modified to test immunomodulatory	pancytopenia, leukopenia, thrombocytopenia, leukemias,
				activity of polypeptides of the invention	Hodgkin's disease, acute lymphocytic anemia (ALL),
				(including antibodies and agonists or	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				antagonists of the invention) include, for	arthritis, AIDS, granulomatous disease, inflammatory
				example, the assays disclosed in Miraglia	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				et al., J Biomolecular Screening 4:193-204	immune reactions to transplanted organs and tissues.
				(1999); Rowland et al., "Lymphocytes: a	hemophilia, hypercoagulation, diabetes mellitus,
				practical approach" Chapter 6:138-160	endocarditis, meningitis, Lyme Disease, inflammation and
				(2000); Mackey et al., J Leukoc Biol	inflammatory disorders, and asthma and allergy.
				63(4):418:428 (1998); and Skov et al.,	
			•	164(7):3500-3505 (2000), the contents of	
				each of which are herein incorporated by	
				reference in its entirety. Human T cells	
				that may be used according to these assays	
				may be isolated using techniques disclosed	
				herein or otherwise known in the art.	
				Human T cells are primary human	
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
236	HLMGP50	750	Upregulation of HLA-	HLA-DR FMAT. MHC class II is essential	Highly preferred indications include blood disorders
			DR and activation of T	for correct presentation of antigen to CD4+	(e.g., as described below under "Immune Activity",
			cells	T cells. Deregulation of MHC class II has	"Blood-Related Disorders", and/or "Cardiovascular

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been associated with autoimmune diseases	Disorders"). Highly preferred indications include
(e.g., diabetes, rheumatoid arthritis,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
systemic lupus erythematosis, and multiple	lupus erythematosis, multiple sclerosis and/or as described
sclerosis). Assays for immunomodulatory	below) and immunodeficiencies (e.g., as described below),
proteins expressed on MHC class II	boosting a T cell-mediated immune response, and
expressing T cells and antigen presenting	alternatively, suppressing a T cell-mediated immune
cells are well known in the art and may be	response. A highly preferred indication is diabetes
used or routinely modified to assess the	mellitus. An additional highly preferred indication
ability of polypeptides of the invention	is a complication associated with diabetes (e.g., diabetic
(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
antagonists of the invention) to modulate	renal failure, nephropathy and/or other diseases and
the activation of T cells, and/or mediate	disorders as described in the "Renal Disorders" section
humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
 immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as
polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
 89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
Gansbacher and Zier, Cell Immunol	complications associated with obesity. Additional highly
117(1):22-34 (1988); and Itoh et al., J	preferred indications include weight loss or alternatively,
Histochem Cytochem 40(11):1675-1683,	weight gain. Aditional highly preferred indications
 the contents of each of which are herein	are complications associated with insulin resistance.
incorporated by reference in its entirety.	Additional highly preferred indications are disorders of the
Human T cells that may be used according	musculoskeletal systems including myopathies, muscular
to these assays may be isolated using	dystrophy, and/or as described herein.

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				known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	additional preferred indication is infection (e.g., AIDS, and/or as described below under "Infectious Disease"). Preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Aldokin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and
237	HLMJB64	751	Activation of transcription through API response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Timmune Activity", "Cardiovascular Disorders", and/or "Blood Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred

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			66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
_			Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
			Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
			85:0342-0346 (1988); Kellahan et al., J	cancer. Other preferred indications include benign
			Siol Chem 2/2(49):30800-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
			Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
			4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
			Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
			contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
			cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
			assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
			the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
			may be used according to these assays	meningitis, and Lyme Disease.
			include the CTLL cell line, which is an IL-	•
			2 dependent suspension-culture cell line	
			with cytotoxic activity.	
237 HLMJB64	751	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g. as
		transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
		cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
		element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
		cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
			antibodies and agonists or antagonists of	æ
			the invention) to increase cAMP and	arthritis, systemic lupus erythematosis, multiple sclerosis
			regulate CREB transcription factors, and	and/or as described below), immunodeficiencies (e.g., as
			modulate expression of genes involved in a	described below), boosting a T cell-mediated immune
			wide variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
			assays for transcription through the cAMP	response. Additional preferred indications include
			response element that may be used or	inflammation and inflammatory disorders. Highly
			routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
			element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
			invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
			agonists or antagonists of the invention)	indications include neoplasms and cancers, such as, for
			include assays disclosed in Berger et al.,	example, leukemia, lymphoma (e.g., T cell lymphoma,
			Gene 66:1-10 (1998); Cullen and Malm,	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
			Methods in Enzymol 216:362-368 (1992);	disease), melanoma, and prostate, breast, lung, colon,
			Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver and urinary

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				85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used	cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, pentrophilia psoriasis suppression of immine reactions to
				according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.	transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
237	HLMJB64	751	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through GAS response element	through the Gamma Interferon Activation Site (GAS) response element are well-	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				antibodies and agonists or antagonists of	Durkit, s lymphoma, non-trodgkins lymphoma, frodgkin s disease), melanoma, and prostate, breast, lung, colon.
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for transcription through the GAS response	such as, for example, hyperplasia, metaplasia, and/or
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include assays disclosed in Berger et al. Gene	Suppressing a 1 cell-mediated immune response. Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,

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			3	4587 (1995), the contents of each of which are herein incorporated by reference in its	scri
				entirety. Exemplary mouse T cells that may be used according to these assays are	is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				used according to these assays include the	prasmacytomas, munipie myetoma, arminis, ALDS, granulomatous disease, inflammatory bowel disease.
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					chocalons, mennglus, Lyme Disease, and asmma and allergy.
237	HLMJB64	751	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
		·		include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred

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237 HLMJB64 751	Activation of transcription through CD28 response element in immune cells (such as T-cells).	the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity. Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, and pypercoagulation, diabetes mellitus, endocarditis, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectiou Bisease."). A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of andor inactivating T cells. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting used or inhibiting the activation of andor inactivating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting sactores and indications include inflammation and inflammatory disorders. Highly preferred indications include inflammaton and inflammatory disorders. Highly preferred immune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, An
		(1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et	additional highly preferred indication includes infection

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			al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma (e.g., metastatic renal cell carcinoma), leukemia, lymphoma (e.g., retastatic renal cell carcinoma), leukemia, lymphoma (e.g., retastatic renal cell carcinoma), leukemia, lymphoma (e.g., retastatic renal cell carcinoma), leukemia, lymphoma (e.g., retal lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is infection (e.g., tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). A highly preferred indications to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, hencythilia, hypercoagulation, diabetes mellius, endocarditis, meningitis, Lyme Disease, asthma and allerev.
238 HLMMX62	(62 752	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the

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assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
invention (including antibodies and	differentiation. An alternative highly preferred
agonists or antagonists of the invention) to	embodiment of the invention includes a method for
promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
activation, and differentiation. Exemplary	
assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
agonists or antagonists of the invention)	rde
include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the

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indications include blood disorders (e.g., neutropenia (and indications include asthma. Highly preferred indications "Cardiovascular Disorders"). Highly preferred indications leukemia), lymphoma (e.g., non-Hodgkin's lymphoma and psoriasis, hemophilia, hypercoagulation, diabetes mellitus, and/or as described below) and immunodeficiencies (e.g., progenitor cells. Preferred indications include boosting leukopenia, thrombocytopenia, acute lymphocytic anemia lung, colon, pancreatic, esophageal, stomach, brain, liver arthritis, systemic lupus erythematosis, multiple sclerosis conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications include: suppression of immune reactions to transplanted organs and tissues (e.g., bone marrow transplant); accelerating and urinary cancer. Other preferred indications include include neoplastic diseases (e.g., leukemia (e.g., acute a T cell-mediated immune response, and alternatively, leukemia, lymphoma, melanoma, and prostate, breast, (ALL), plasmacytomas, multiple myeloma, Burkitt's Hodgkin's disease), and/or as described below under patients), and/or as described below under "Immune benign dysproliferative disorders and pre-neoplastic also include autoimmune diseases (e.g., rheumatoid indications include neoplasms and cancers, such as, Preferred indications include anemia, pancytopenia, endocarditis, meningitis, Lyme Disease, and allergy. the prevention of neutropenia (e.g., in HIV infected lymphoma, arthritis, AIDS, granulomatous disease, "Hyperproliferative Disorders"). Highly preferred as described below). Additional highly preferred inflammatory bowel disease, sepsis, neutrophilia, myeloid recovery; and mobilizing hematopoietic suppressing a T cell-mediated immune response. lymphoblastic leukemia, and acute myelogenous Activity", "Blood-Related Disorders", and/or agonists or antagonists of the invention) to known in the art. Natural killer (NK) cells mediate immunomodulation and modulate production of cytokines, such as GM-CSF, cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of eukocytes. Exemplary assays that test for assays are publicly available (e.g., through and the activation of T cells. Such assays the invention) include the assays disclosed Chapter 6:138-160 (2000); and Ye et al., J Leukoc Biol (58(2):225-233, the contents that may be used or routinely modified to immunomodulatory proteins evaluate the Screening 4:193-204 (1999); Rowland et by reference in its entirety. Natural killer an important role in the differentiation of increases antigen presentation. GM-CSF cytokine. Assays for immunomodulatory antibodies and agonists or antagonists of cells that may be used according to these are large granular lymphocytes that have of each of which are herein incorporated polypeptides of the invention (including al., "Lymphocytes: a practical approach" techniques disclosed herein or otherwise proteins that promote the production of assess the ability of polypeptides of the GM-CSF are well known in the art and is considered to be a proinflammatory may be used or routinely modified to the ATCC) or may be isolated using invention (including antibodies and test immunomodulatory activity of dendritic cells and monocytes, and in Miraglia et al., J Biomolecular the growth and differentiation of

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				tumor cells and also recognize antibody	
				bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.	
240	HLQCL64	754	Upregulation of CD69	CD69 FMAT. CD69 is an activation	A highly preferred embodiment of the invention
		-	and activation of T cells	marker that is expressed on activated T	includes a method for activating T cells. An alternative
·-				cells, B cells, and NK cells. CD69 is not	highly preferred embodiment of the invention includes a
				expressed on resting T cells, B cells, or	method for inhibiting the activation of and/or inactivating
				NK cells. CD69 has been found to be	T cells. A highly preferred embodiment of the
				associated with inflammation. Assays for	invention includes a method for activation B cells. An
				immunomodulatory proteins expressed in	alternative highly preferred embodiment of the invention
				T cells, B cells, and leukocytes are well	includes a method for inhibiting the activation of and/or
				known in the art and may be used or	inactivating B cells. A highly preferred embodiment
				routinely modified to assess the ability of	of the invention includes a method for activating NK cells.
				polypeptides of the invention (including	An alternative highly preferred embodiment of the
			,	antibodies and agonists or antagonists of	invention includes a method for inhibiting activation of
				the invention) to modulate the activation of	and/or inactivation NK cells. Highly preferred
				T cells, and/or mediate humoral or cell-	indications include inflammation and inflammatory
				mediated immunity. Exemplary assays	disorders (e.g., as described below under "Immune
				that test for immunomodulatory proteins	Activity"). Preferred indications include blood
				evaluate the upregulation of cell surface	disorders (e.g., as described below under "Immune
				markers, such as CD69, and the activation	Activity", "Blood-Related Disorders", and/or
		••••		of T cells. Such assays that may be used	"Cardiovascular Disorders"). Highly preferred indications
				or routinely modified to test	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory activity of	systemic lupus erythematosis, multiple sclerosis and/or as
				polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
		,		antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
				the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
				assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
				Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
				Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
		•		approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
				Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
				(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
				(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
				Afetra et al., Ann Rheum Dis 52(6):457-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,

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			are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preparationed.	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, inflammation and inflammatory disorders, asthma, and allergies. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms, such as, for example, leukemia,
			inmunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
241 HLQCX36	755	Activation of Skeletal Mucle Cell P13 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention
			metabolism and cell survivial are well- known in the art and may be used or routinely modified to assess the ability of	includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a
			polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival.	specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell proliferation. In a specific embodiment, skeletal muscle
			Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase-induced activity of polypeptides of the invention (including	cell proliferation is inhibited. A preferred embodiment of the invention includes a method for stimulating muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is stimulated. An alternative
			the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes	highly preferred embodiment of the invention includes a method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is inhibited. Highly preferred indications include disorders
			49(2):263-2/1 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety.	of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), endocrine disorders (e.g.,
			Rat myoblast cells that may be used	as described below under Endocrine Disorders"), neural disorders (e.g., as described below under "Neural Activity

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according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
 available (e.g., through the ATCC). Exemplary rat myoblast cells that may be	described below under "Immune Activity", "Cardiovascular Discreters" and/or "Blood Delated
used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
cells. L6 is an adherent rat myoblast cell	under "Immune Activity"), and infection (e.g., as
 line, isolated from primary cultures of rat	described below under "Infectious Disease"). A
thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus. An
multinucleated myotubes and striated	additional highly preferred indication is a complication
tibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
	diabetic nephropathy, kidney disease (e.g., renal failure,
	nephropathy and/or other diseases and disorders as
	described in the "Renal Disorders" section below), diabetic
	neuropathy, nerve disease and nerve damage (e.g., due to
	diabetic neuropathy), blood vessel blockage, heart disease,
	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infections (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below, especially of the urinary tract and
	skin), carpal tunnel syndrome and Dupuytren's
	contracture). An additional highly preferred indication
	is obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	ons are co
	insulin resistance. Additional highly preferred
	indications are disorders of the musculoskeletal system
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	described herein. Additional highly preferred

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HLWAF06 756 Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its	indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart diseases, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural
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	be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
	publicly available (e.g., through the	described below under "Intectious Disease"). A highly preferred indication is diabetes mellities.
	that may be used according to these assays	ation
	include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
-		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and
		impaired wound healing, infection (e.g., infectious
		diseases and disorders as described in the "Infectious
		sec
		and skin). An additional highly preferred indication is
		obesity and/or complications associated with obesity.
		ndicat
		or alternatively, weight gain. Additional highly
		ons are
		insulin resistance. Additional highly preferred
		indications are disorders of the musculoskeletal systems
		including myopathies, muscular dystrophy, and/or as
		described herein. Additional highly preferred
		indications include, hypertension, coronary artery disease,
		dyslipidemia, gallstones, osteoarthritis, degenerative
		arthritis, eating disorders, fibrosis, cachexia, and kidney
		diseases or disorders. Preferred indications include
		neoplasms and cancer, such as, lymphoma, leukemia and

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breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely
	Production of ICAM-1	Production of ICAM-1
	757	758
	HLWAU42	HLWAU42
	243	244

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				modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	
542	HLWAV47	759	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,
				cells that may be used according to these	incianoma, gnoma (e.g., mangnant gnoma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal.

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				the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
246	HLWBB73	760	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate modulate T cell proliferation and function.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cell-mediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include sashma and allerery Highly preferred indications include sashma and allerery Highly preferred indications include

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				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
			•	modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	infe
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
247	HLWCN37	761		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	invention includes a method for inhibiting the production
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
		_		IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").

brain, liver and urinary cancer. Other preferred indications neutrophilia, psoriasis, suppression of immune reactions to immunodeficiency (e.g., as described below), boosting a T thrombocytopenia, Hodgkin's disease, acute lymphocytic disease, inflammatory bowel disease, sepsis, neutropenia, Highly preferred indications include autoimmune disease cell-mediated immune response, and suppressing a T cell mediated immune response. Additional highly preferred (e.g., rheumatoid arthritis, systemic lupus erythematosis, example, leukemia, lymphoma, melanoma, and prostate, neoplastic conditions, such as, for example, hyperplasia, lymphoma, melanoma, and/or as described below under indications include neoplasms and cancers, such as, for indications include neoplastic diseases (e.g., leukemia, metaplasia, and/or dysplasia. Preferred indications breast, lung, colon, pancreatic, esophageal, stomach, Burkitt's lymphoma, arthritis, AIDS, granulomatous indications include inflammation and inflammatory disorders. Additional preferred indications include anemia (ALL), plasmacytomas, multiple myeloma, "Hyperproliferative Disorders"). Highly preferred include benign dysproliferative disorders and preidiopathic pulmonary fibrosis. Highly preferred hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. multiple sclerosis and/or as described below). transplanted organs and tissues, hemophilia, include anemia, pancytopenia, leukopenia, (Oxford) 38(3):214-20 (1999), the contents Chapter 6:138-160 (2000); Gonzalez et al., agonists or antagonists of the invention) to production of cytokines, such as Interferon by reference in its entirety. Human T cells nelper cell functions are well known in the Billiau et al., Ann NY Acad Sci 856:22-32 that may be used according to these assays may be isolated using techniques disclosed ymphocytes that mature in the thymus and to assess the ability of polypeptides of the the invention) include the assays disclosed art and may be used or routinely modified immunomodulatory proteins evaluate the (1998); Boehm et al., Annu Rev Immunol Screening 4:193-204 (1999); Rowland et express a T Cell receptor and CD3, CD4, polypeptides of the invention (including antibodies and agonists or antagonists of of each of which are herein incorporated al., "Lymphocytes: a practical approach" or CD8. These cells mediate humoral or gamma (IFNg), and the activation of T 15:749-795 (1997), and Rheumatology inflammatory activities, modulate TH2 cells. Such assays that may be used or mediate immunomodulation, regulate J Clin Lab Anal 8(5):225-233 (1995); herein or otherwise known in the art. nvention (including antibodies and helper cell function, and/or mediate humoral or cell-mediated immunity. Human T cells are primary human in Miraglia et al., J Biomolecular immunomodulatory activity of Exemplary assays that test for routinely modified to test

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				cell-mediated imminity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
248	HLWDB73	762	Activation of Skeletal	Kinase assay. Kinase assays, for examplek	Highly preferred indications include endocrine
			Muscle Cell ERK	Elk-1 kinase assays, for ERK signal	disorders (e.g., as described below under "Endocrine
			Signalling Pathway	transduction that regulate cell proliferation	Disorders") and disorders of the musculoskeletal system.
				or differentiation are well known in the art	Preferred indications include neoplastic diseases (e.g., as
				and may be used or routinely modified to	described below under "Hyperproliferative Disorders"),
				assess the ability of polypeptides of the	blood disorders (e.g., as described below under "Immune
				invention (including antibodies and	Activity", "Cardiovascular Disorders", and/or "Blood-
				agonists or antagonists of the invention) to	Related Disorders"), immune disorders (e.g., as described
				promote or inhibit cell proliferation,	below under "Immune Activity"), neural disorders (e.g., as
				activation, and differentiation. Exemplary	described below under "Neural Activity and Neurological
				assays for ERK kinase activity that may be	Diseases"), and infection (e.g., as described below under
				used or routinely modified to test ERK	"Infectious Disease"). A highly preferred indication
				kinase-induced activity of polypeptides of	
				the invention (including antibodies and	indication is a complication associated with diabetes (e.g.,
		•		agonists or antagonists of the invention)	diabetic retinopathy, diabetic nephropathy, kidney disease
				include the assays disclosed in Forrer et	(e.g., renal failure, nephropathy and/or other diseases and
				al., Biol Chem 379(8-9):1101-1110	disorders as described in the "Renal Disorders" section
				(1998); Le Marchand-Brustel Y, Exp Clin	below), diabetic neuropathy, nerve disease and nerve
				Endocrinol Diabetes 107(2):126-132	damage (e.g., due to diabetic neuropathy), blood vessel
				(1999); Kyriakis JM, Biochem Soc Symp	blockage, heart disease, stroke, impotence (e.g., due to
				64:29-48 (1999); Chang and Karin, Nature	diabetic neuropathy or blood vessel blockage), seizures,
				410(6824):37-40 (2001); and Cobb MH,	mental confusion, drowsiness, nonketotic hyperglycemic-
				Prog Biophys Mol Biol 71(3-4):479-500	hyperosmolar coma, cardiovascular disease (e.g., heart
				(1999); the contents of each of which are	disease, atherosclerosis, microvascular disease,
				herein incorporated by reference in its	hypertension, stroke, and other diseases and disorders as
				entirety. Rat myoblast cells that may be	described in the "Cardiovascular Disorders" section
				used according to these assays are publicly	below), dyslipidemia, endocrine disorders (as described in
				available (e.g., through the ATCC).	the "Endocrine Disorders" section below), neuropathy,
				Exemplary rat myoblast cells that may be	vision impairment (e.g., diabetic retinopathy and
				used according to these assays include L6	blindness), ulcers and impaired wound healing, infection
				cells. L6 is an adherent rat myoblast cell	(e.g., infectious diseases and disorders as described in the
				line, isolated from primary cultures of rat	"Infectious Diseases" section below, especially of the
				thigh muscle, that fuses to form	urinary tract and skin), carpal tunnel syndrome and
	į,			multinucleated myotubes and striated	Dupuytren's contracture). An additional highly

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			antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
			the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
-			Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
			(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
			Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
			Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
			865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
			Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
	=		Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
			Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
			of each of which is herein incorporated by	with insulin resistance.
			reference in its entirety. Pancreatic cells	
			that may be used according to these assays	
			are publicly available (e.g., through the	
			ATCC) and/or may be routinely generated.	
			Exemplary pancreatic cells that may be	
			used according to these assays include	
		*** ··-	HITT15 Cells. HITT15 are an adherent	
			epithelial cell line established from Syrian	
			hamster islet cells transformed with SV40.	
			These cells express glucagon,	
			somatostatin, and glucocorticoid receptors.	
			The cells secrete insulin, which is	
			stimulated by glucose and glucagon and	
			suppressed by somatostatin or	
			glucocorticoids. ATTC# CRL-1777	
			Refs: Lord and Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc. Natl. Acad.	
+			Sci. USA 78: 4339-4343, 1981.	
250 HLYEU59	764	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
		transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
		AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune
		in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
		as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
			antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
			the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
			other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,

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				element that may be used or routinely	imminodeficiencies (a a se described below) Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
		_		(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
		•		Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
			•	85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety.	anemia (ALL), plasmacytomas, multiple myeloma,
				Mouse T cells that may be used according	Burkitt's lymphoma, granulomatous disease, inflammatory
				to these assays are publicly available (e.g.,	bowel disease, sepsis, psoriasis, suppression of immune
				through the ATCC). Exemplary mouse T	reactions to transplanted organs and tissues, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease.
				assays include the HT2 cell line, which is	•
				an IL-2 dependent suspension culture cell	
\dashv				line that also responds to IL-4.	
251 H	HLYGB19	765	Activation of Skeletal	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			Mucle Cell PI3 Kinase	an GSK-3 kinase assay, for PI3 kinase	includes a method for increasing muscle cell survival An
		•	Signalling Pathway	signal transduction that regulate glucose	alternative highly preferred embodiment of the invention
_				metabolism and cell survivial are well-	includes a method for decreasing muscle cell survival.
				known in the art and may be used or	A preferred embodiment of the invention includes a
				routinely modified to assess the ability of	method for stimulating muscle cell proliferation. In a
				polypeptides of the invention (including	specific embodiment, skeletal muscle cell proliferation is
				antibodies and agonists or antagonists of	stimulated. An alternative highly preferred embodiment of
				the invention) to promote or inhibit	the invention includes a method for inhibiting muscle cell
				glucose metabolism and cell survival.	proliferation. In a specific embodiment, skeletal muscle
				Exemplary assays for PI3 kinase activity	cell proliferation is inhibited. A preferred embodiment
				that may be used or routinely modified to	of the invention includes a method for stimulating muscle
				test PI3 kinase-induced activity of	cell differentiation. In a specific embodiment, skeletal

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				skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal system including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions,
251 HLYGB19	765	Upregulation of CD152 and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cells. T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and

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				modulate the activation of T cells	suppressing a T cell-mediated immine response
				maintain T cell homeostasis and/or	Highly preferred indications include neonlastic diseases
				manitali i cen nomeostasis, and or	inging presence indications include neopiastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
				immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
_				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
	-			are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
252	HLYGE16	992	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
				(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
		,	in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,

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	to I collect	ability of nolynentides of the invention	increasing) TNF alpha production Preferred indications
	•	(including antibodies and agonists or	ွှ
		antagonists of the invention) to bind the	"Immune Activity", "Blood-Related Disorders", and/or
		serum response factor and modulate the	"Cardiovascular Disorders"), Highly preferred indications
		expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
		and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
		related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
		Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
		the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
		modified to test SRE activity of the	immune response. Additional highly preferred indications
		polypeptides of the invention (including	include inflammation and inflammatory disorders, and
		antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
		the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
		Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
		and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
		368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
		Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
		Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
		3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
		12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
		of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
		reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
		be used according to these assays are	pre-neoplastic conditions, such as, for example,
		publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
		ATCC). Exemplary human T cells, such	indications include anemia, pancytopenia, leukopenia,
		as the MOLT4, that may be used according	thrombocytopenia, Hodgkin's disease, acute lymphocytic
		to these assays are publicly available (e.g.,	anemia (ALL), plasmacytomas, multiple myeloma,
		through the ATCC).	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			disease, inflammatory bowel disease, neutropenia,
			neutrophilia, psoriasis, suppression of immune reactions to
			transplanted organs and tissues, hemophilia,
			hypercoagulation, diabetes mellitus, endocarditis,
			meningitis, Lyme Disease, cardiac reperfusion injury, and
			asthma and allergy. An additional preferred indication
			is infection (e.g., an infectious disease as described below
252 HLYGE16 766	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy. Another

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			transcription through STAT6 response	through the Signal Transducers and Activators of Transcription (STAT6)	highly preferred indication is asthma. Additional highly preferred indications include inflammation and
			element in immune	response element are well-known in the art	inflammatory disorders. Preferred indications
			cells (such as natural	and may be used or routinely modified to	include blood disorders (e.g., as described below under
			killer cells).	assess the ability of polypeptides of the	"Immune Activity", "Blood-Related Disorders", and/or
				invention (including antibodies and	"Cardiovascular Disorders"). Preferred indications include
				agonists or antagonists of the invention) to	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				regulate STAT6 transcription factors and	lupus erythematosis, multiple sclerosis and/or as described
				modulate the expression of multiple genes.	below) and immunodeficiencies (e.g., as described below).
				Exemplary assays for transcription through	Preferred indications include neoplastic diseases (e.g.,
				the STAT6 response element that may be	leukemia, lymphoma, melanoma, and/or as described
				used or routinely modified to test STAT6	below under "Hyperproliferative Disorders"). Preferred
				response element activity of the	indications include neoplasms, such as, for example,
				polypeptides of the invention (including	leukemia, lymphoma, melanoma, and prostate, breast,
				antibodies and agonists or antagonists of	lung, colon, pancreatic, esophageal, stomach, brain, liver
				the invention) include assays disclosed in	and urinary cancer. Other preferred indications include
				Berger et al., Gene 66:1-10 (1998); Cullen	benign dysproliferative disorders and pre-neoplastic
				and Malm, Methods in Enzymol 216:362-	conditions, such as, for example, hyperplasia, metaplasia,
				368 (1992); Henthorn et al., Proc Natl	and/or dysplasia. Preferred indications include
				Acad Sci USA 85:6342-6346 (1988);	enia, leukop
				Georas et al., Blood 92(12):4529-4538	Hodgkin's disease, acute lymphocytic anemia (ALL),
				(1998); Moffatt et al., Transplantation	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				69(7):1521-1523 (2000); Curiel et al., Eur	arthritis, AIDS, granulomatous disease, inflammatory
				J Immunol 27(8):1982-1987 (1997); and	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				Masuda et al., J Biol Chem	suppression of immune reactions to transplanted organs
				275(38):29331-29337 (2000), the contents	and tissues, hemophilia, hypercoagulation, diabetes
				of each of which are herein incorporated	mellitus, endocarditis, meningitis, and Lyme Disease.
				by reference in its entirety. T cells that	Additional preferred indications include infection (e.g., an
				may be used according to these assays are	infectious disease as described below under "Infectious
				publicly available (e.g., through the	Disease").
				ATCC). Exemplary rat natural killer cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC).	
253	HLYGY91	192	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,

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	antihodies and agonists or antagonists of	nantronathy and/or other diseases and discardances
	the invention) to stimulate insulin	described in the "Renal Disorders" section helow) diabetic
	secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
	is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease.
	insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
	pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
	glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
	proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
	key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
	assays that may be used or routinely	stroke, and other diseases and disorders as described in the
	modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
-	secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
	polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
	antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
	the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
	Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
	(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
	Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
	Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
	865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
	Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
	Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
	Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
	of each of which is herein incorporated by	with insulin resistance.
	reference in its entirety. Pancreatic cells	
	that may be used according to these assays	
	are publicly available (e.g., through the	
	ATCC) and/or may be routinely generated.	
	Exemplary pancreatic cells that may be	
	used according to these assays include	
	HITT15 Cells. HITT15 are an adherent	
	epithelial cell line established from Syrian	
	hamster islet cells transformed with SV40.	
	These cells express glucagon,	
	somatostatin, and glucocorticoid receptors.	
	The cells secrete insulin, which is	

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				stimulated by alucose and alucasan and	
_				suppressed by somatostatin or	
				glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
254	HMCAZ04	768	Activation of Adinocyte	Kinase assay Kinase assays for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay for FRK signal	includes a method for stimulating adinocyte proliferation
			Pathway	transduction that regulate cell proliferation	includes a memora for summaring authoryte prometation: An alternative highly preferred embodiment of the
			`	or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	'n
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
,				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
_				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
_				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	described below under "Infectious Disease").
				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
				that may be used according to these assays	additional highly preferred indication is a complication
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,

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	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and
		impaired wound healing, infection (e.g., infectious
		diseases and disorders as described in the "Infectious
		Diseases" section below (particularly of the urinary tract
		and skin). An additional highly preferred indication is
		obesity and/or complications associated with obesity.
		Additional highly preferred indications include weight loss
		or alternatively, weight gain. Additional highly
		ns are
		insulin resistance. Additional highly preferred
		indications are disorders of the musculoskeletal systems
		hies,
		described herein. Additional highly preferred
		indications include, hypertension, coronary artery disease,
		dyslipidemia, gallstones, osteoarthritis, degenerative
		arthritis, eating disorders, fibrosis, cachexia, and kidney
-		diseases or disorders. Preferred indications include
		neoplasms and cancer, such as, lymphoma, leukemia and
		breast, colon, and kidney cancer. Additional preferred
		indications include melanoma, prostate, lung, pancreatic,
		esophageal, stomach, brain, liver, and urinary cancer.
		Highly preferred indications include lipomas and
		liposarcomas. Other preferred indications include benign

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HMCAZ04	769	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH,	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine Disorders (e.g., as described below under "Endocrine Disorders"). Preferred below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below.
			Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation	under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetes (e.g., diabetic retinopathy, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic

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	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate differentiation conditions known in the art.	graphic neuropaury), prood vesser processes, near unsease, stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and
		impaired wound healing, infection (e.g., infectious
		diseases and disorders as described in the "Infectious
		Diseases" section below (particularly of the urinary tract
		and skin). An additional highly preferred indication is
		obesity and/or complications associated with obesity.
		Additional highly preferred indications include weight loss
		or alternatively, weight gain. Additional highly
		preferred indications are complications associated with
		insulin resistance. Additional highly preferred
		indications are disorders of the musculoskeletal systems
		including myopathies, muscular dystrophy, and/or as
		described herein. Additional highly preferred
		indications include, hypertension, coronary artery disease,
		dyslipidemia, gallstones, osteoarthritis, degenerative
		arthritis, eating disorders, fibrosis, cachexia, and kidney
		diseases or disorders. Preferred indications include
		neoplasms and cancer, such as, lymphoma, leukemia and
		breast, colon, and kidney cancer. Additional preferred
		indications include melanoma, prostate, lung, pancreatic,
		esophageal, stomach, brain, liver, and urinary cancer.
-		Highly preferred indications include lipomas and
		liposarcomas. Other preferred indications include benign
		dysproliferative disorders and pre-neoplastic conditions,
		such as, for example, hyperplasia, metaplasia, and/or
		dysplasia.

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256 HMCAZ04	770	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Bipphys Mol Biol 71(3-4):479-500	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below, under "Immune Activity", "Cardiovascular Disorders",
			(1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation conditions known in the art.	and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or

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blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious Diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication sasociated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, each as and pre-enablasia and/or as and pre-enablasia.	dysplasia. A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the
	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation
	Activation of Adipocyte ERK Signaling Pathway
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or differentiation are well known in the art	invention includes a method for inhibiting adjuncted
and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
assess the ability of polypeptides of the	ą
invention (including antibodies and	differentiation. An alternative highly preferred
agonists or antagonists of the invention) to	embodiment of the invention includes a method for
promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,

athe strol "Cat "Cat "Cat "Cat "Cat "Cat "Cat "Cat	Activation of Adipocyte Kinase assay. Kinase assay, for example ERK Signaling an Elk-1 kinase assay, for ERK signal Pathway Pathway and may be used or routinely modified to assess the ability of polypeptides of the invention includes a method for stimulating adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation.
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	invention (including antibodies and	differentiation. An alternative highly preferred
	agonists or antagonists of the invention) to	embodiment of the invention includes a method for
	promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
	activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
•	assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
	used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
	kinase-induced activity of polypeptides of	o uo
	the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
	agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
	include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
	al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
	(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
	Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
	(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
	64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
	410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
	Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
	(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
	herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
	entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
٠	be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
	publicly available (e.g., through the	described below under "Infectious Disease").
	ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
	that may be used according to these assays	additional highly preferred indication is a complication
	include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,

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				endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
259 НМСFН60	773	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and

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				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10.(1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
		_		Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
		_		Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
	•			contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
				with cytotoxic activity.	
259	HIMCFH60	773	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described

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				activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response, and additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allerey.
259	НМСЕН60	773	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as,

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				Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectiou (e.g., an infectious disease as described below under "Infectious Disease").
260	HMDAB29	774	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the

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"Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or
used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ohtani KI, et al., Endocrinology, 139(1):172-8 (1998); Krautheim A, et al, Exp Clin Endocrinol Diabetes, 107 (1):29-34 (1999), the contents of each of which is herin incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. 178A 78- 4339-4343, 1981	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from
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stimulated by glucose and glucagon and suppressed by somatostatin or
glucocorticoids. A11C# CKL-1/// Refs: Lord and Ashcroft. Biochem. J. 219:
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54/-55]; Santerre et al. Proc. Natl. Acad.

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A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stifnulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) immunodeficiancies (e.g., e.g., described below) immunodeficiancies (e.g., e.g., described	described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, inflammation and inflammatory disorders, and asthma and allergy. An
CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204	(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which
Upregulation of CD152 and activation of T cells		
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				are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	additional preferred indication is infection (e.g., as described below under "Infectious Disease").
261	HMDAD44	775	Regulation of transcription via DMEF1 response element in adipocytes and pre-adipocytes	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetes (e.g., diabetic rephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious biseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with

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weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cells that continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation culture conditions.	MCP-I FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis,
	Production of MCP-1
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				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
			-	Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
				contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
				according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or
				using techniques disclosed herein or	dysplasia.
				otherwise known in the art. Human	
				dendritic cells are antigen presenting cells	
				in suspension culture, which, when	
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
				and functional activities.	
261	HMDAD44	775	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-

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	Toutinely infomited to assess the ability of	Related Disolucis, allufor Cardiovascular Disolucis),
	polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
	antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
	the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
	immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
	inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
	assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
	proteins evaluate the production of	Additional highly preferred indications include
	cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
	alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
	inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
	response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
-	routinely modified to test	leukemia, lymphoma, and/or as described below under
	immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
	polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
	antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
	the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
	Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
	4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
	"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
	Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
	al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
-	(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
	160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
	al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
	Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
	(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
	herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
	entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
	be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
	isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
	or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
	dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
	in suspension culture, which, when	Disease").
	activated by antigen and/or cytokines,	
	initiate and upregulate T cell proliferation	
	and functional activities.	

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			such as include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, cells. Such leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple atory and myeloma, Burkitt's lymphoma arthritis, Alm			norated by such as, for example, hyperplasia, metaplasia, and/or n dendritic dysplasia. g to these chniques
MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell	chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate	macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and	chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	(2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of	each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques
Production of MIP1alpha						
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				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
263	HMEDE24	777	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			NFAT response	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
			element in immune	known in the art and may be used or	Disorders"). Highly preferred indications include
			cells (such as T-cells).	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
				antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),
				the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
				transcription factors and modulate	suppressing a T cell-mediated immune response.
				expression of genes involved in	Additional highly preferred indications include
				immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
				assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
				response element that may be used or	disease as described below under "Infectious Disease").
				routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.

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				AICC). Exemplary human I cells that	
				may be used according to these assays	
				include the SUPT cell line, which is a	
				suspension culture of IL-2 and IL-4	
				responsive T cells.	
264	HIMEDI90	778	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription of Malic	of Malic Enzyme are well-known in the art	An additional highly preferred indication is a complication
			Enzyme in adipocytes	and may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,
				assess the ability of polypeptides of the	diabetic nephropathy, kidney disease (e.g., renal failure,
				invention (including antibodies and	nephropathy and/or other diseases and disorders as
				agonists or antagonists of the invention) to	described in the "Renal Disorders" section below), diabetic
				regulate transcription of Malic Enzyme, a	neuropathy, nerve disease and nerve damage (e.g., due to
				key enzyme in lipogenesis. Malic enzyme	diabetic neuropathy), blood vessel blockage, heart disease,
				is involved in lipogenesisand its expression	stroke, impotence (e.g., due to diabetic neuropathy or
				is stimulted by insulin. ME promoter	blood vessel blockage), seizures, mental confusion,
				contains two direct repeat (DR1)- like	drowsiness, nonketotic hyperglycemic-hyperosmolar
				elements MEp and MEd identified as	coma, cardiovascular disease (e.g., heart disease,
				putative PPAR response elements. ME	atherosclerosis, microvascular disease, hypertension,
				promoter may also responds to AP1 and	stroke, and other diseases and disorders as described in the
				other transcription factors. Exemplary	"Cardiovascular Disorders" section below), dyslipidemia,
				assays that may be used or routinely	endocrine disorders (as described in the "Endocrine
				modified to test for regulation of	Disorders" section below), neuropathy, vision impairment
				transcription of Malic Enzyme (in	(e.g., diabetic retinopathy and blindness), ulcers and
				adipoocytes) by polypeptides of the	impaired wound healing, and infection (e.g., infectious
				invention (including antibodies and	diseases and disorders as described in the "Infectious
				agonists or antagonists of the invention)	Diseases" section below, especially of the urinary tract and
				include assays disclosed in: Streeper, R.S.,	tunne
				et al., Mol Endocrinol, 12(11):1778-91	contracture). An additional highly preferred
				(1998); Garcia-Jimenez, C., et al., Mol	indication is obesity and/or complications associated with
				Endocrinol, 8(10):1361-9 (1994); Barroso,	obesity. Additional highly preferred indications include
				I., et al., J Biol Chem, 274(25):17997-8004	weight loss or alternatively, weight gain. Aditional
				(1999); Ijpenberg, A., et al., J Biol Chem,	highly preferred indications are complications associated
				272(32):20108-20117 (1997); Berger, et	with insulin resistance.
				al., Gene 66:1-10 (1988); and, Cullen, B.,	
				et al., Methods in Enzymol. 216:362-368	
			-	(1992), the contents of each of which is	
				herein incorporated by reference in its	

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				entirety. Hepatocytes that may be used	
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				hepatocytes that may be used according to	
				these assays includes the H4IIE rat liver	
				hepatoma cell line.	
265 HI	HMELM75	977	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that are	includes a method for stimulating (e.g., increasing) MCP-1
				produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
				to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
				monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as
				modified to assess the ability of	described below under "Infectious Disease"). Additional
				polypeptides of the invention (including	highly preferred indications include inflammation and
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
•				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,

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266 HMIAK10	780	Activation of transcription through GAS response element in immune cells (such as T-cells).	contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response	pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune disease (e.g., thermatoid archivits systemic lunus
			element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998), Cullen and Malm, Methods in Enzymol 216:362-368 (1992), Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its	ouseases (e.g., meumatoita artifitus, systemic tupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Tmmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication

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		entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and
266 HMIAK10	 Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur	A highly preferred indication is allergy. A highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitic Lymphoma, arthritic Almanhoma, anthritic almannia
		Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to

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				by reference in its entirety. T cells that	uanspianted organs and ussues, nemopinita, hypercoagulation, diabetes mellitus, endocarditis.
				may be used according to these assays are	meningitis, and Lyme Disease. An additional
				publicly available (e.g., through the	preferred indication is infection (e.g., an infectious disease
				ATCC). Exemplary T cells that may be	as described below under "Infectious Disease").
				used according to these assays include the	
				SUPT cell line, which is a suspension	
\dashv				culture of IL-2 and IL-4 responsive T cells.	
766	HMIAK10	780	Activation of	Assays for the activation of transcription	Highly preferred indications include inflammation and
			transcription through	through the NFKB response element are	inflammatory disorders. Highly preferred indications
			NFKB response	well-known in the art and may be used or	include blood disorders (e.g., as described below under
			element in immune	routinely modified to assess the ability of	"Immune Activity", "Blood-Related Disorders", and/or
			cells (such as T-cells).	polypeptides of the invention (including	"Cardiovascular Disorders"). Highly preferred indications
-				antibodies and agonists or antagonists of	include autoimmune diseases (e.g., rheumatoid arthritis,
				the invention) to regulate NFKB	systemic lupus erythematosis, multiple sclerosis and/or as
				transcription factors and modulate	described below), and immunodeficiencies (e.g., as
				expression of immunomodulatory genes.	described below). An additional highly preferred
				Exemplary assays for transcription through	indication is infection (e.g., AIDS, and/or an infectious
				the NFKB response element that may be	disease as described below under "Infectious Disease").
				used or rountinely modified to test NFKB-	Highly preferred indications include neoplastic diseases
				response element activity of polypeptides	(e.g., melanoma, leukemia, lymphoma, and/or as described
				of the invention (including antibodies and	below under "Hyperproliferative Disorders"). Highly
				agonists or antagonists of the invention)	preferred indications include neoplasms and cancers, such
				include assays disclosed in Berger et al.,	as, melanoma, renal cell carcinoma, leukemia, lymphoma,
				Gene 66:1-10 (1998); Cullen and Malm,	and prostate, breast, lung, colon, pancreatic, esophageal,
				Methods in Enzymol 216:362-368 (1992);	stomach, brain, liver and urinary cancer. Other preferred
				Henthorn et al., Proc Natl Acad Sci USA	indications include benign dysproliferative disorders and
				85:6342-6346 (1988); Black et al., Virus	pre-neoplastic conditions, such as, for example,
				Gnes 15(2):105-117 (1997); and Fraser et	hyperplasia, metaplasia, and/or dysplasia. Preferred
				al., 29(3):838-844 (1999), the contents of	indications also include anemia, pancytopenia, leukopenia,
				each of which are herein incorporated by	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				reference in its entirety. T cells that may	anemia (ALL), plasmacytomas, multiple myeloma,
				be used according to these assays are	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia,
				ATCC). Exemplary human T cells that	neutrophilia, psoriasis, hemophilia, hypercoagulation,
				may be used according to these assays	diabetes mellitus, endocarditis, meningitis, Lyme Disease,
				include the SUPT cell line, which is a	suppression of immune reactions to transplanted organs,

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				suspension culture of IL-2 and IL-4	asthma and allergy.
330	UNITAVIO	700	A cetitotion of	Account for the activities of transmission	A mentioned ambidiment of the invention includes
007	HMIAKIO	08/	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Kesponse Element	method for inhibiting (e.g., reducing), I'NF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
				used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			-	NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,

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				nypercoagulation, diagrees mentions, endocardings, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
267 HMIBF07	781	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reduction.) MCP-1 production. A highly preferred embodiment of indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes and tissues, hemophilia, hypercoagulation, diabetes also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary

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and continue to the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability diabot of polypeptides of the invention (including antibodies and agonists or antagonists of the invention is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulated by drow glucose and also by certain proteins/peptides, and disregulation is a ather assays that may be used or routinely modified to test for stimulation of insulin secretion from pancreatic beta cells by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by the pancreation of insulin secretion (from pancreatic cells) by the	lated
in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention is measured by FMAT using anti-rat insulin accretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J. 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8): 305-17 (1999); Fliipsson, K., et al., Ann N Y Acad Sci, 865-41-1 (1989); Olson, L.K., et al., Brio Chem. 2711/28-15644-57 (1906); and Brio Chem. 2711/28-15644-57 (1906); and 2711/28-15644-57 (190	sciosed nerein or dyspiasia. The art. Human intigen presenting cells
activated by antigen and or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIBEO7 781 Insulin Secretion Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention is measured by FMAT using anti-rat insulin actetion is measured by FMAT using anti-rat insulin activition pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H, et al., Endocr, 1, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K, et al., Ann N Y Acad Sci, 865:41-4 (1998); Olson, L.K., et al., J Briof, Phan, 27(1904); All All Chem, 27(1908); Disclassing and 2005-2006.	re, which, when
HMIBFO7 781 Insulin Secretion Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J. 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865-41.4 (1998); Olson, L.K., et al., Brid Chem. 2711(28): 154-457 (1904).	n and/or cytokines,
HMIBFO7 781 Insulin Secretion The are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J. 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrino, 13(8):1303-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865-41.4 (1998); Olson, L.K., et al., Brid Chem 2011060; and Brid	ate 1 cen promeration
are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Fliipsson, K., et al., Ann N Y Acad Sci, 865-441-4 (1998); Olson, L.K., et al., J	
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pu	skin), carpal tunne
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•	, obesity. Additional highly preferred indications i
	04 (1999), the contents highly preferred indications are complications associated

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267 HMIBF07 781	reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. ISBA 78: 4339-4343, 1981.	Stimulation of insulin are well-known in the art and may be used pancreatic beta cells. or routinely modified to assess the ability of polypeptides of the invention (including annibodies and agonists or antagonists of methopathy, kidney disease (e.g., renal failure, antibodies and agonists or antagonists of methopathy, kidney disease (e.g., renal failure, neuropathy, kidney disease (e.g., renal failure, ascretion. For example, insulin secretion is measured by FMAT using anti-rat part of the invention) to stimulate insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is assays that may be used or routinely modified to test for stimulation of insulin antibodies and agonists or antagonists of the invention) include assays disclosed in:
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 (2000); Nor et al., J Vasc Res 37(3): 209- embodiment of the invention includes a method for 218 (2000); and Karsan and Harlan, J reducing cardiac hypertrophy. An alternative highly are herein for inducing cardiac hypertrophy. Highly preferred	 sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells which line blood vessels and other part of the process of the pro	•

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example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", and infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indication is include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilla, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus.	endocarditis, meningitis, Lyme Disease, and asthma and allergy. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic
polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+T cells. Deregulation of MHC class II has been associated with autoimmune diseases (e.g., diabetes, rheumatoid arthritis,
as T-cells).	Upregulation of HLA- DR and activation of T cells
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lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and alternatively, suppressing a T cell-mediated immune response. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel	diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel	syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. An additional preferred indication is infection (e.g., AIDS, and/or as described below under "Infectious Disease").
systemic lupus erythematosis, and multiple sclerosis). Assays for immunomodulatory proteins expressed on MHC class II expressing T cells and antigen presenting cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for	upregulation of MHC class II products, such as HLA-DR antigens, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Lamour et al., Clin Exp Immunol	89(2):217-222 (1992); Hurme and Sihvola, Immunol Lett 20(3):217-222 (1989); Gansbacher and Zier, Cell Immunol 117(1):22-34 (1988); and Itoh et al., J Histochem Cytochem 40(11):1675-1683, the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are
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				primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and
270	HMJAK70	784	Proliferation, and/or cytokine production in immune cells (such as T-cells).	Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, differentiation., and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer.

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			(2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakamoto H, et al., J Biol Chem, 275(46):35857-35862 (2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the	
271 HMSBE04	785	Activation of transcription through	mouse CTLL cell line. Assays for the activation of transcription through the AP1 response element are	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"),
		AP1 response element in immune cells (such	known in the art and may be used or routinely modified to assess the ability of	blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-
		as T-cells).	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and	Kelated Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases.
			other cell functions. Exemplary assays for transcription through the API response	(e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
			element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
			modified to test AP1-response element activity of polypeptides of the invention	highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications
			(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
			antagonists of the invention) include assays disclosed in Berger et al., Gene	lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred
			66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
			Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci USA	leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary
			85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
		-	Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
			Chang et al., Mol Cell Biol 10(9):4900- 4993 (1998); and Fraser et al., Eur J	such as, for example, hyperphasia, incraphasia, and/or dysplasia. Preferred indications include arthritis,
			Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
			contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
			cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
			assays are publicly available (e.g., through the ATCC) Exemplary mouse T cells that	bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis
			the ATCC). Exemplary mouse I cells that	reactions to transplanted organs and tissues, endocarditis,

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meningitis, and Lyme Disease.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Autoimmunity, Allergy and Asthma
may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438 (1998); Pyatt DW, et al., Cell Biol Toxicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al., Immunology 90(3):455-460 (1997); Aramburau et al., 1 Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicity available (e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the Reh
	Activation of transcription through NFKB response element in immune cells (such as B-cells).
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		We have		B-cell line.	
273	HMSCR69	787	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that are	includes a method for stimulating (e.g., increasing) MCP-1
				produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
				to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
				monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as
				modified to assess the ability of	described below under "Infectious Disease"). Additional
				polypeptides of the invention (including	=
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
			+++	Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
				contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
				according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or
				using techniques disclosed herein or	dysplasia.
				otherwise known in the art. Human	

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			dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities	
274 HMSHC86	788	Activation of Skeletal Muscle Cell ERK Signalling Pathway	Kinase assays, for examplek Elk-1 kinase assays, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cells.	Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders") and disorders of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Implection (e.g., as described below under "Infectious Disease"). A highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (e.g., heart diseases and impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infection diseases and disorders as described in the "Endocrine disorders as

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				thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include heast, rabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Highly preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperalistia metaplasia and/or dysplasia
275	HMSHU20	789	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T immunodeficiency (e.g., as described below), boosting a T

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			agonists or antagonists of the invention) to	cell-mediated immine response, and suppressing a T cell-
			mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
			inflammatory activities, modulate TH2	indications include inflammation and inflammatory
			helper cell function, and/or mediate	disorders. Additional preferred indications include
			humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
			Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
			immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
			production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
			gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
			cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
			routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
			immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
			polypeptides of the invention (including	include benign dysproliferative disorders and pre-
			antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
			the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
			in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
			Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
			Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
			Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
			(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
			15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
			Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
			of each of which are herein incorporated	
			by reference in its entirety. Human T cells	
			that may be used according to these assays	
			may be isolated using techniques disclosed	
			herein or otherwise known in the art.	
			Human T cells are primary human	
			lymphocytes that mature in the thymus and	
			express a T Cell receptor and CD3, CD4,	
			or CD8. These cells mediate humoral or	
			cell-mediated immunity and may be	
			preactivated to enhance responsiveness to	
			immunomodulatory factors.	
276 HMSHY25 790	ا	Production of GM-CSF	GM-CSF FMAT. GM-CSF is expressed	A highly preferred embodiment of the invention

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hy noticited T nelle morrowhere	includes a method for stimulating the production of GM.
endothelial cells, and fibroblasts. GM-	CSF. An alternative highly preferred embodiment of the
CSF regulates differentiation and	invention includes a method for inhibiting the production
 proliferation of granulocytes- macrophage	of GM-CSF. Highly preferred indications include
 progenitors and enhances antimicrobial	inflammation and inflammatory disorders. An additional
activity in neutrophils, monocytes and	highly preferred indication is infection (e.g., as described
macrophage. Additionally, GM-CSF plays	below under "Infectious Disease". Highly preferred
an important role in the differentiation of	indications include blood disorders (e.g., neutropenia (and
dendritic cells and monocytes, and	the prevention of neutropenia (e.g., in HIV infected
increases antigen presentation. GM-CSF	patients), and/or as described below under "Immune
 is considered to be a proinflammatory	Activity", "Blood-Related Disorders", and/or
cytokine. Assays for immunomodulatory	"Cardiovascular Disorders"). Highly preferred indications
proteins that promote the production of	also include autoimmune diseases (e.g., rheumatoid
GM-CSF are well known in the art and	arthritis, systemic lupus erythematosis, multiple sclerosis
may be used or routinely modified to	and/or as described below) and immunodeficiencies (e.g.,
assess the ability of polypeptides of the	as described below). Additional highly preferred
 invention (including antibodies and	indications include asthma. Highly preferred indications
 agonists or antagonists of the invention) to	include neoplastic diseases (e.g., leukemia (e.g., acute
 mediate immunomodulation and modulate	lymphoblastic leukemia, and acute myelogenous
the growth and differentiation of	leukemia), lymphoma (e.g., non-Hodgkin's lymphoma and
leukocytes. Exemplary assays that test for	Hodgkin's disease), and/or as described below under
immunomodulatory proteins evaluate the	"Hyperproliferative Disorders"). Highly preferred
production of cytokines, such as GM-CSF,	indications include neoplasms and cancers, such as,
and the activation of T cells. Such assays	leukemia, lymphoma, melanoma, and prostate, breast,
that may be used or routinely modified to	lung, colon, pancreatic, esophageal, stomach, brain, liver
test immunomodulatory activity of	and urinary cancer. Other preferred indications include
polypeptides of the invention (including	benign dysproliferative disorders and pre-neoplastic
antibodies and agonists or antagonists of	conditions, such as, for example, hyperplasia, metaplasia,
the invention) include the assays disclosed	and/or dysplasia. Highly preferred indications include:
in Miraglia et al., J Biomolecular	suppression of immune reactions to transplanted organs
Screening 4:193-204 (1999); Rowland et	and tissues (e.g., bone marrow transplant); accelerating
al., "Lymphocytes: a practical approach"	myeloid recovery; and mobilizing hematopoietic
 Chapter 6:138-160 (2000); and Ye et al., J	progenitor cells. Preferred indications include boosting
Leukoc Biol (58(2):225-233, the contents	a T cell-mediated immune response, and alternatively,
of each of which are herein incorporated	suppressing a T cell-mediated immune response.
by reference in its entirety. Natural killer	Preferred indications include anemia, pancytopenia,
cells that may be used according to these	leukopenia, thrombocytopenia, acute lymphocytic anemia

				assays are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell, mediated extotoxicity	(ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy.
276	HMSHY25	790	Production of IFNgamma using Natural Killer cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2; promotes IgG2a and inhibits IgE; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" (e.g. cancer/tumorigenesis) and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing antibody-dependent immune responses, suppressing antibody-dependent immune responses, boosting innate immunity and immune responses, and suppressing innate immunity and immune responses. Additional highly preferred indications include idiopathic pulmonary fibrosis. Highly preferred indications include indiopathic pulmonary fibrosis. Highly preferred indications include indiopathic pulmonary
				immunomodulatory activity of polypeptides of the invention (including	diseases (e.g., leukemia, lymphoma, meianoma, and/or as described below under "Hyperproliferative Disorders").

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			antibodies and agonists or antagonists of	Highly preferred indications include neoplasms and
			the invention) include the assays disclosed	cancers, such as, for example, leukemia, lymphoma,
			in Miraglia et al., J Biomolecular	melanoma, and prostate, breast, lung, colon, pancreatic,
			Screening 4:193-204 (1999); Rowland et	esophageal, stomach, brain, liver and urinary cancer.
			al., "Lymphocytes: a practical approach"	Other preferred indications include benign dysproliferative
			Chapter 6:138-160 (2000); Gonzalez et al.,	disorders and pre-neoplastic conditions, such as, for
			J Clin Lab Anal 8(5):225-233 (1995);	example, hyperplasia, metaplasia, and/or dysplasia.
			Billiau et al., Ann NY Acad Sci 856:22-32	Preferred indications include anemia, pancytopenia,
-			(1998); Boehm et al., Annu Rev Immunol	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			15:749-795 (1997), and Rheumatology	lymphocytic anemia (ALL), plasmacytomas, multiple
			(Oxford) 38(3):214-20 (1999), the contents	myeloma, Burkitt's lymphoma, arthritis, AIDS,
			of each of which are herein incorporated	granulomatous disease, inflammatory bowel disease,
			by reference in its entirety. Natural Killer	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			(NK) cells that may be used according to	immune reactions to transplanted organs and tissues,
			these assays are publicly available (e.g.,	hemophilia, hypercoagulation, diabetes mellitus,
			through the ATCC) or may be isolated	endocarditis, meningitis, Lyme Disease, asthma and
			using techniques disclosed herein or	allergy.
			otherwise known in the art. Natural killer	i
			(NK) cells are large granular lymphocytes	
			that have cytotoxic activity but do bind	
			antigen. NK cells show antibody-	
			independent killing of tumor cells and also	
			recognize antibody bound on target cells,	
			via NK Fc receptors, leading to cell-	
			mediated cytotoxicity.	
277 HMTAB77	791	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
		transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
		serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
		in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
		as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
			the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
			growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
			transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
			used or routinely modified to test SKE	(e.g., as described below), boosting a T cell-mediated

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2/8 HMUAE26	792	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly

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of timore is associated with timor	preferred embodiment of the invention includes a method
 regression due to loss of tumor blood	for stimulating apontosis of endothelial cells. An
regression due to 1055 of tuition proof	
supply. Exemplary assays for caspase	
apoptosis that may be used or routinely	includes a method for inhibiting (e.g
modified to test capase apoptosis activity	
of polypeptides of the invention (including	
antibodies and agonists or antagonists of	
the invention) include the assays disclosed	osed embodiment of the invention includes a method for
in Lee et al., FEBS Lett 485(2-3): 122-126	-126 inhibiting angiogenesis. A highly preferred
(2000); Nor et al., J Vasc Res 37(3): 209-	
 218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
 Atheroscler Thromb 3(2): 75-80 (1996);	
the contents of each of which are herein	in for inducing cardiac hypertrophy. Highly preferred
incorporated by reference in its entirety.	
Endothelial cells that may be used	
according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
sources). Exemplary endothelial cells that	
 may be used according to these assays	
include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
endothelial cells which line blood vessels	sels overload, and/or as described below under
and are involved in functions that include,	ude, / "Cardiovascular Disorders"). Highly preferred indications
but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
vascular permeability, vascular tone, and	
immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
	themselves, such as of the arteries, capillaries, veins and/or
	lymphatics). Highly preferred are indications that
	stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,
•	bacillary angiomatosis, hemangioendothelioma,

				angiosarcoma, haemangiopericytoma, lymphangioma,
				lymphangiosarcoma. Highly preferred indications also
	•			include cancers such as, prostate, breast, lung, colon,
				pancreatic, esophageal, stomach, brain, liver, and urinary
				cancer. Preferred indications include benign
				dysproliferative disorders and pre-neoplastic conditions,
	-			such as, for example, hyperplasia, metaplasia, and/or
				dysplasia. Highly preferred indications also include
		•		arterial disease, such as, atherosclerosis, hypertension,
				coronary artery disease, inflammatory vasculitides,
	•			Reynaud's disease and Reynaud's phenomenom,
				aneurysms, restenosis; venous and lymphatic disorders
				such as thrombophlebitis, lymphangitis, and lymphedema;
				and other vascular disorders such as peripheral vascular
				disease, and cancer. Highly preferred indications also
				æ
				(e.g., vascular injury such as, injury resulting from balloon
				angioplasty, and atheroschlerotic lesions), implant
				fixation, scarring, ischemia reperfusion injury, rheumatoid
				arthritis, cerebrovascular disease, renal diseases such as
				acute renal failure, and osteoporosis. Additional highly
				preferred indications include stroke, graft rejection,
	-			diabetic or other retinopathies, thrombotic and coagulative
				disorders, vascularitis, lymph angiogenesis, sexual
				disorders, age-related macular degeneration, and treatment
				/prevention of endometriosis and related conditions.
				Additional highly preferred indications include fibromas,
				heart disease, cardiac arrest, heart valve disease, and
				vascular disease. Preferred indications include blood
				disorders (e.g., as described below under "Immune
				Activity", "Blood-Related Disorders", and/or
				"Cardiovascular Disorders"). Preferred indications include
				autoimmune diseases (e.g., rheumatoid arthritis, systemic
•				lupus erythematosis, multiple sclerosis and/or as described
			44.00	below) and immunodeficiencies (e.g., as described below).
				Additional preferred indications include inflammation and
				inflammatory disorders (such as acute and chronic

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					inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
278	HMUAE26	792		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preterred embodiment of the
				cytokine. IFNg promotes TH1 and	incl
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
				helper cell functions are well known in the	Highly preferred indications include autoimmune disease
				art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
				invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
				agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
			* <u></u>	mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
			~	inflammatory activities, modulate TH2	indications include inflammation and inflammatory
				helper cell function, and/or mediate	disorders. Additional preferred indications include
				humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
				Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
				immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
				production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
				gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
				cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
				routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
				immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
				polypeptides of the invention (including	include benign dysproliferative disorders and pre-
				antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
				the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
				in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
				Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
				Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				J CIIII Lao Anai 8(3):223-233 (1993);	disease, initammatory bower disease, sepsis, neuropenia,

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				Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
279	HMUAN45	793	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al.,	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and

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				Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
280	HMVBC31	794	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment

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(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune
antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(10):4589-601 (1995);Mogami H, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary
	Activation of transcription through cAMP response element in immune cells (such as T-cells).
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response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic retinopathy, diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, attoke, and other diseases and disorders as described in the
assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the HT2 cell line, which is a suspension culture of IL-2 dependent T cells that also respond to IL-4.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or
	Regulation of apoptosis in pancreatic beta cells.
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"Can endo Disc (e.g. weight high high with high high high high with with with with high with high high high high high high high h	A highly preferred embodiment of the invention s secreted by includes a method for inhibiting (e.g., reducing) IL-5 production. An alternative highly preferred embodiment of osinophil the invention includes a method for stimulating (e.g.,
antagonists of the invention) include the assays disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al., Biochem Mol Biol Int, 39(6):1229-36 (1996); Krautheim, A., et al., Br J Pharmacol, 129(4):687-94 (2000); Chandra J, et al., Diabetes, 50 Suppl 1:S44-7 (2001); Suk K, et al., J Immunol, 166(7):4481-9 (2001); Tejedo J, et al., FEBS Lett, 459(2):238-43 (1999); Zhang, S., et al., FEBS Lett, 459(2):238-43 (1999); Zhang, S., et al., FEBS Lett, 459(2):238-43 (1999); Zhang, S., et al., FEBS Lett, 455(3):315-20 (1999); Lee et al., FEBS Lett, 455(3):315-20 (1999); Lee et al., FEBS Lett, 455(3):315-30 (1996); the contents of each of which are herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1980 77:3519.	IL-5 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells, mast cells, basophils, and eosinophils that stimulate eosinophil
	Production of IL-5
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	function and B cell Ig production and	increasing) IL-5 production. A highly preferred
	promote polarization of CD4+ cells into	Ξ
	TH2 cells are well known in the art and	stimulating (e.g., increasing) immunoglobulin production.
	may be used or routinely modified to	An alternative highly preferred embodiment of the
	assess the ability of polypeptides of the	invention includes a method for inhibiting (e.g.,
	invention (including antibodies and	decreasing) immunoglobulin production. A highly
	agonists or antagonists of the invention) to	
	mediate immunomodulation, stimulate	
	immune cell function, modulate B cell Ig	preferred indication includes rhinitis. An additional
	production, modulate immune cell	highly preferred indication is infection (e.g., an infectious
	polarization, and/or mediate humoral or	disease as described below under "Infectious Disease"),
	cell-mediated immunity. Exemplary	and inflammation and inflammatory disorders.
	assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
	proteins evaluate the production of	described below under "Immune Activity", "Blood-
	cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
	stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
-	cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
	be used or routinely modified to test	multiple sclerosis and/or as described below) and
-	immunomodulatory activity of	immunodeficiencies (e.g., as described below).
	polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
	antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
	the invention) include the assays disclosed	below under "Hyperproliferative Disorders"). Preferred
	in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
	Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
	al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
	Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include
	Blood 92(9):3338-3345 (1998); Jung et al.,	benign dysproliferative disorders and pre-neoplastic
	Eur J Immunol 25(8):2413-2416 (1995);	conditions, such as, for example, hyperplasia, metaplasia,
	Mori et al., J Allergy Clin Immunol 106(1	and/or dysplasia. Preferred indications include anemia,
	Pt 2):558-564 (2000); and Koning et al.,	pancytopenia, leukopenia, thrombocytopenia, leukemias,
	Cytokine 9(6):427-436 (1997), the	Hodgkin's disease, acute lymphocytic anemia (ALL),
	contents of each of which are herein	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
	incorporated by reference in its entirety.	arthritis, AIDS, granulomatous disease, inflammatory
	Human T cells that may be used according	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
	to these assays may be isolated using	immune reactions to transplanted organs and tissues,
	techniques disclosed herein or otherwise	hemophilia, hypercoagulation, diabetes mellitus,
	known in the art. Human I cells are	endocarditis, meningitis, and Lyme Disease.

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				primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	•
284 HINE	HNEAK81	798	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., 1 Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednh 45(1):9-19 (2001); Drakes et	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such the disease include neoplasms and cancers, such below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such the disease in the property of the disease include neoplasms and cancers, such the disease include include neoplasms and cancers, such the disease includes include neoplasms and cancers, such the disease includes include neoplasms and cancers, such disease includes include and disease.
				al., 1 ransp 1mmunol 8(1):1/-29 (2000); Verhasselt et al., J Immunol 158:2919-	as, leukemia, 19mpnoma, prostate, oreast, 1ung, coton, pancreatic, esophageal, stomach, brain, liver, and urinary

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				publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia,
				ATCC). Exemplary numan 1 cells that	neutrophilia, psoriasis, nemophilia, nypercoagulation,
				inay be used according to mese assays include the SUPT cell line, which is a	ulabetes inclinus, endocal ditis, inclinigus, Lynie Disease, suppression of immune reactions to transplanted organs,
				suspension culture of IL-2 and IL-4	asthma and allergy.
ì	or mount	000		responsive 1 cells.	
780	HNECW49	800	Proliferation,	Kinase assays, for example kinase assays	Preferred embodiments of the invention include using
			differentiation, and/or	for members of the MAP kinase family	polypeptides of the invention (or antibodies, agonists, or
			cytokine production in	(including p38, JAK, and ERK) are well	antagonists thereof) in detection, diagnosis, prevention,
			immune cells (such as	known in the art and may be used or	and/or treatment of inflammation, infection, allergy,
			T-cells).	routinely modified to assess the ability of	asthma, autoimmunity, and cancer.
				polypeptides of the invention (including	
				antibodies and agonists or antagonists of	
				the invention) to promote or inhibit cell	
				proliferation, differentiation., and/or	
				cytokine production in immune cells such	
				as T-cells. Exemplary assays for MAP	
				kinase family members that may be used	
			-	or routinely modified to test polypeptides	
				of the invention (including antibodies and	
				agonists or antagonists of the invention)	
				include the assays disclosed in: Rincon M.,	
				Curr Opin Immunol; 13(3):339-345	
				(2001); Wang LH, et al., J Immunol,	
				162(7):3897-3904 (1999); Sakamoto H, et	
				al., J Biol Chem, 275(46):35857-35862	
				(2000), the contents of each of which are	
				herein incorporated by reference in its	
				entirety. Exemplary immune cells (for	
				example, T-cells) that may be used	
				according to these assays include the	
				mouse CTLL cell line.	
287	HNEDH88	801	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune
			in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
			as I-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious

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				antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
				the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
-				transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
				with cytotoxic activity.	
288	HNFAC50	. 708	Regulation of apoptosis	Caspase Apoptosis. Assays for caspase	Preferred embodiments of the invention include using
			of immune cells (such	apoptosis are well known in the art and	polypeptides of the invention (or antibodies, agonists, or
			as mast cells).	may be used or routinely modified to	antagonists thereof) in detection, diagnosis, prevention,
				assess the ability of polypeptides of the	and/or treatment of asthma, allergy, hypersensitivity and
				invention (including antibodies and	inflammation.
				agonists or antagonists of the invention) to	
				regulate caspase protease-mediated	
				apoptosis in immune cells (such as, for	
				example, in mast cells). Mast cells are	
				found in connective and mucosal tissues	

HNFGR08 80	803	Regulation of viability and proliferation of	throughout the body, and their activation via immunoglobulin E -antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells in vitro are well-human mast cell line.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g. diabetic retinonally)
		pancreatic beta cells.	known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent	associated with tradetts (e.g., tradetts fettinopatity, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or

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				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
				viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
				regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
				invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
				agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
				include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
				BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
				(2001); Huotari MA, et al., Endocrinology,	tunne
				139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
				Biol Chem 1998 Jul 10;273(28):17771-9	indication is obesity and/or complications associated with
				(1998), the contents of each of which is	obesity. Additional highly preferred indications include
				herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
				entirety. Pancreatic cells that may be used	highly preferred indications are complications associated
				according to these assays are publicly	with insulin resistance.
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
290	HNFHF34	804	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention
			MIP1alpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An
				activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
				monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
				chemotaxis are well known in the art and	production. A highly preferred indication is infection
				may be used or rounnery mounted to	(c.g., an infectious disease as described below under

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				assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
				invention (including antibodies and	blood disorders (e.g., as described below under "Immune
				agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
				mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
				chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
				differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
				for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
				the production of chemokines, such as	described below). Additional highly preferred indications
				macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
					Preferred indications also include anemia, pancytopenia,
	- (monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
				modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
				invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
				include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
				J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
				a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
				Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	-
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
		_		cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
291 HNGAK51	ζ51 805	2	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.

described in the "Renal Disorders" section below), diabetic An additional highly preferred indication is a complication stroke, and other diseases and disorders as described in the Diseases" section below, especially of the urinary tract and diabetic neuropathy), blood vessel blockage, heart disease, Disorders" section below), neuropathy, vision impairment neuropathy, nerve disease and nerve damage (e.g., due to "Cardiovascular Disorders" section below), dyslipidemia, indication is obesity and/or complications associated with highly preferred indications are complications associated diabetic nephropathy, kidney disease (e.g., renal failure, obesity. Additional highly preferred indications include impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious stroke, impotence (e.g., due to diabetic neuropathy or atherosclerosis, microvascular disease, hypertension, drowsiness, nonketotic hyperglycemic-hyperosmolar (e.g., diabetic retinopathy and blindness), ulcers and endocrine disorders (as described in the "Endocrine blood vessel blockage), seizures, mental confusion, nephropathy and/or other diseases and disorders as associated with diabetes (e.g., diabetic retinopathy, coma, cardiovascular disease (e.g., heart disease, An additional highly preferred skin), carpal tunnel syndrome and Dupuytren's weight loss or alternatively, weight gain. with insulin resistance. contracture). of polypeptides of the invention (including Biol Chem, 271(28):16544-52 (1996); and, are well-known in the art and may be used Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents that may be used according to these assays ATCC) and/or may be routinely generated. epithelial cell line established from Syrian of each of which is herein incorporated by hamster islet cells transformed with SV40. or routinely modified to assess the ability insulin antibodies. Insulin secretion from the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 secretion. For example, insulin secretion modified to test for stimulation of insulin antibodies and agonists or antagonists of antibodies and agonists or antagonists of reference in its entirety. Pancreatic cells polypeptides of the invention (including proteins/peptides, and disregulation is a HITT15 Cells. HITT15 are an adherent key component in diabetes. Exemplary are publicly available (e.g., through the Exemplary pancreatic cells that may be Filipsson, K., et al., Ann N Y Acad Sci. 865:441-4 (1998); Olson, L.K., et al., J pancreatic beta cells is upregulated by used according to these assays include assays that may be used or routinely is measured by FMAT using anti-rat (2000); Salapatek, A.M., et al., Mol secretion (from pancreatic cells) by Endocrinol, 13(8):1305-17 (1999); the invention) to stimulate insulin These cells express glucagon, glucose and also by certain

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				somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. 178. A 78. 4330, 434.	
292 I	HNGAM58	908	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperprolasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	<u>-</u>

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				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis. AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
292	HNGAM58	908	Upregulation of CD152	CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention
			and activation of T cells	expression is restricted to activated T cells.	includes a method for activating T cells. An alternative
				CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				proliferation. Reduced CD152 expression	method for inhibiting the activation of and/or inactivating
				has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
				autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
				CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
				immunoresponses. Assays for	of the invention includes a method for stimulating T cell
				immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
				expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
				CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications
				may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
				assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
				invention (including antibodies and	described below), immunodeficiencies (e.g., as described
				agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
				modulate the activation of T cells,	suppressing a T cell-mediated immune response.
				maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
				immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for

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exam Preference Preference Preference Preference Preference Preference Preference Preference Brann Bra	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include inflammation and inflammatory
(including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include
	Activation of transcription through CD28 response element in immune cells (such as T-cells).
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assays disclosed in Berger et al., Gene	disorders. Highly preferred indications include
66:1-10 (1998); Cullen and Malm,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. An
 (1997); Parra et al., J Immunol	additional highly preferred indication includes infection
166(4):2437-2443 (2001); and Butscher et	(e.g., AIDS, and/or as described below under "Infectious
al., J Biol Chem 3(1):552-560 (1998), the	Disease"). Highly preferred indications include
contents of each of which are herein	neoplastic diseases (e.g., melanoma, renal cell carcinoma,
incorporated by reference in its entirety. T	leukemia, lymphoma, and/or as described below under
cells that may be used according to these	"Hyperproliferative Disorders"). Highly preferred
assays are publicly available (e.g., through	indications include neoplasms and cancers, such as, for
the ATCC). Exemplary human T cells that	example, melanoma (e.g., metastatic melanoma), renal cell
may be used according to these assays	carcinoma (e.g., metastatic renal cell carcinoma),
include the JURKAT cell line, which is a	leukemia, lymphoma (e.g., T cell lymphoma), and
suspension culture of leukemia cells that	prostate, breast, lung, colon, pancreatic, esophageal,
produce IL-2 when stimulated.	stomach, brain, liver and urinary cancer. Other preferred
	indications include benign dysproliferative disorders and
	pre-neoplastic conditions, such as, for example,
	hyperplasia, metaplasia, and/or dysplasia. A highly
	preferred indication is infection (e.g., tuberculosis,
	infections associated with granulomatous disease, and
	osteoporosis, and/or an infectious disease as described
	below under "Infectious Disease"). A highly preferred
	indication is AIDS. Additional highly preferred
	indications include suppression of immune reactions to
	transplanted organs and/or tissues, uveitis, psoriasis, and
	tropical spastic paraparesis. Preferred indications
	include blood disorders (e.g., as described below under
	"Immune Activity", "Blood-Related Disorders", and/or
	"Cardiovascular Disorders"). Preferred indications also
	include anemia, pancytopenia, leukopenia,
	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	anemia (ALL), plasmacytomas, multiple myeloma,
	Burkitt's lymphoma, arthritis, granulomatous disease,
	inflammatory bowel disease, sepsis, neutropenia,

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					neutrophilia, hemophilia, hypercoagulation, diabetes
					mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
294	HNGDQ38	808	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that are	includes a method for stimulating (e.g., increasing) MCP-1
				produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
				to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
				monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as
				modified to assess the ability of	described below under "Infectious Disease"). Additional
				polypeptides of the invention (including	highly preferred indications include inflammation and
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
	•			production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
	-			monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
			-	cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
		,		contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
				according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or